PB81-126716

Terrazole: Pesticide Registration Standard
5-Ethoxy-3-trichloromethyl-1,2,4-thiadiazole

(U.S.) Environmental Protection Agency
Arlington, VA

Sep 80

U.S. Department of Commerce
National Technical Information Service
NTIS

United States
Environmental Protection
Agency

Office of
Pesticides and Toxic Substances
Washington DC 20460

September 1980

PB81-126716

Pesticides

EPA

5-Ethoxy-3-trichloromethyl - 1,2,4-thiadiazole

Terrazole

Pesticide Registration Standard

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA 22161

50272-101

REPORT DOCUMENTATION PAGE

1. REPORT NO.
EPA/OPP-80/525

2.

3. Recipient's Accession No.

4. Title and Subtitle
Terrazole: Pesticide Registration Standard

5. Report Date
9/80

6.

7. Author(s)

8. Performing Organization Rept. No.

9. Performing Organization Name and Address
Environmental Protection Agency
Special Pesticide Review Division
Crystal Mall #2
Arlington, VA. 22202

10. Project/Task/Work Unit No.

11. Contract(C) or Grant(G) No.
(C)
(G)

12. Sponsoring Organization Name and Address
Environmental Protection Agency
401 M St. S.W.
Washington, D.C. 20460

13. Type of Report & Period Covered

14.

15. Supplementary Notes

16. Abstract (Limit: 200 words)

A comprehensive statement of the Agency's regulatory position on all pesticide products containing the same active ingredient. The document discribes the data upon which the regulatory position is based, provides the rationale for the position and states the conditions which must be met to register a product under a standard.

17. Document Analysis a. Descriptors
0504,0606,0703

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

18. Availability Statement:
Unlimited

19. Security Class (This Report)
Unclassified

20. Security Class (This Page)
Unclassified

21. No. of Pages

22. Price

(See ANSI-Z39.18)

See Instructions on Reverse

OPTIONAL FORM 272 (4-77)
(Formerly NTIS-35)
Department of Commerce

ATTENTION

PORTIONS OF THIS REPORT ARE NOT LEGIBLE. HOWEVER, IT IS THE BEST REPRODUCTION AVAILABLE FROM THE COPY SENT TO NTIS.

Registration Standard
for
Products Containing the
Single Active Ingredient Terrazole^R

Gregory A. Thies, Project Manager (SPRD)
Hank Appleton, Environmental Chemist (HED, EFB)
Diane Beavers, Product Manager (RD)
William Boodee, Chemist (HED, RCB)
Rodger Gardner, Toxicologist (HED, TB)
Robert Holst, Plant Physiologist (HED, EEB)
John Tice, Wildlife Biologist (HED, EEB)

A special thanks is extended to Donna Peacher, Jerry Moore and Juanita Wills for their assistance during this project.

September, 1980

Office of Pesticides and Toxic Substances

Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

TABLE OF CONTENTS

Page

Chapter 1 - How to Register Under a Registration Standard

Organization of the Standard 1
Purpose of the Standard 1
Requirements for Re-registration Under the Standard 3
"Product specific" Data and "Generic" Data 3
Data Compensation Requirements Under FIFRA 3(c)(1)(D) 4
Obtaining Data to Fill "Data Gaps;" FIFRA 3(c)(2)(B) 5
Amendments to the Standard 6

Chapter 2 - Regulatory Position
Introduction

Generic Data Requirements 8
Manufacturing-Use Terrazole 12
End-Use Formulations of Terrazole 13

Chapter 3 - Product Chemistry
Topical Discussions

Chemical Identity 25
Manufacturing Process 26
Formation of Unintentional Ingredients 27
Percentages of Active Ingredient 27
Product Analytical Methods and Data 29
Physical Chemical Properties 29

Disciplinary Review

Chemistry Profile 31
Generic Data Gaps 31
Suggested Labeling 32
Bibliography 33

Chaper 4 - Environmental Fate

Use Profile 34

Topical Discussions

Physico-Chemical Transformation 35
Metabolism 36
Mobility 45
Field Dissipation 47
Accumulation 48

Disciplinary Review

Environmental Fate Profile 51
Exposure Profile 53
Generic Data Gaps 55
Suggested Labeling 55
Bibliography 56

Chapter 5 - Toxicology

Topical Discussions

Metabolism and Pharmacodynamics 58
Acute Effects and Neurotoxicity 62
Subchronic Effects and Neurotoxicity 69
Chronic Effects 71
Oncogenicity 72
Mutagenicity 72
Teratology 73
Reproductive Effects 75
Emergency Treatment 75

Disciplinary Review

Toxicology Profile 76
Toxicology Hazard Assessment 79
Generic Data Gaps 79
Suggested Labeling 80
Bibliography 82

Chapter 6 - Residue Chemistry

Topcial Discussions

Metabolism in Plants 85
Metabolism in Animals 86
Analytical Methods 86
Residue Data 87
Present Tolerances 88
Regulatory Incidents 88

Disciplinary Review

Residue Chemistry Profile 89
Reassessment of Established Tolerances 89
Generic Data Gaps 90
Bibliography 91

Chapter 7 - Ecological Effects

Topical Discussions

Birds 92
Wild Mammals 92
Aquatic Invertebrates 93
Fish 93
Ecosystem Effects 93

Disciplinary Review

Ecological Effects Profile 94
Hazard Assessment 94
Generic Data Gap 94
Suggested Labeling 95
Bibliography 96

Chapter 8 - Regulatory Rationale

Product Composition Standards 98
Acute Toxicity Limits 98
Use Patterns 99
Data Requirements 99
Required Labeling 99

Bibliography

Guide to Use of This Bibliography 99
Citations Considered to be Part of the Data Base Supporting Registration of This Standard 101
Citations Judged to be Inappropriate for Use in Developing This Standard 109
Standard Reference Material 116

CHAPTER 1

HOW TO REGISTER UNDER A REGISTRATION STANDARD

Reproduced from best available copy.

Organization of the Standard
Purpose of the Standard
Requirement to Re-register Under the Standard
"Product Specific" Data and "Generic" Data
Data Compensation Requirements under FIFRA 3(c)(1)(D)
Obtaining Data to Fill "Data Gaps"; FIFRA 3(c)(2)(B)
Amendments to the Standard

Organization of the Standard

This first chapter explains the purpose of a Registration Standard and summarizes the legal principles involved in registering or re-registering under a Standard. The second chapter sets forth the requirements that must be met to obtain or retain registration for products covered by this particular Registration Standard. In the remaining chapters, the Agency reviews the available data by scientific discipline, discusses the Agency's concerns with the identified potential hazards, and logically develops the conditions and requirements that would reduce those hazards to acceptable levels.

Purpose of the Standard

Section 3 of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) provides that "no person in any State may distribute, sell, offer for sale, hold for sale, ship, deliver for shipment, or receive (and having so received) deliver or offer to deliver, to any person any pesticide which is not registered with the Administrator [of EPA]." To approve the registration of a pesticide, the Administrator must find, pursuant to Section 3(c)(5) that:

> "(A) its composition is such as to warrant the proposed claims for it;
> (B) its labeling and other material required to be submitted comply with the requirements of this Act;
> (C) it will perform its intended function without unreasonable adverse effects on the environment; and
> (D) when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment."

In making these findings, the Agency reviews a wide range of data which registrants are required to submit, and assesses the risks and benefits associated with the use of the proposed pesticide. But the established approach to making these findings has been found to be defective on two counts:

First, EPA and its predecessor agency, the United States Department of Agriculture (USDA), routinely reviewed registration applications on a 'product by product' basis, evaluating each product-specific application somewhat independently. In the review of products containing similar components, there was little opportunity for a retrospective review of the full range of pertinent data available in Agency files and in the public literature. Thus the 'product by product' approach was often inefficient and sometimes resulted in inconsistent or incomplete regulatory judgments.

Second, over the years, as a result of inevitable and continuing advancesin scientific knowledge, methodology, and policy, the data base for many pesticides came to be considered inadequate by current scientific and regulatory standards. Given the long history of pesticide regulation in several agencies, it is even likely that materials may have been lost from the data files. When EPA issued new requirements for registration in 1975 (40 CFR 162) and proposed new guidelines for hazard testing in 1978 (43 FR 29686, July 10, 1978 and 43 FR 37336, August 22, 1978), many products that had already been registered for years were being sold and used without the same assurances of human and environmental safety as was being required for new products. Because of this inconsistency, Congress directed EPA to re-register all previously registered products, so as to bring their registrations and their data bases into compliance with current requirements [See FIFRA Section 3(g)].

Facing the enormous job of re-reviewing and calling-in new data for the approximately 35,000 current registrations, and realizing the inefficiencies of the 'product by product' approach, the Agency decided that a new, more effective method of review was needed.

A new review procedure has been developed. Under it, EPA publishes documents called Registration Standards, each of which discusses a particular pesticide active ingredient. Each Registration Standard summarizes all the data available to the Agency on a particular active ingredient and its current uses, and sets forth the Agency's comprehensive position on the conditions and requirements for registration of all existing and future products which contain that active ingredient. These conditions and requirements, all of which must be met to obtain or retain full registration or re-registration under Section 3(c)(5) of FIFRA, include the submission of needed scientific data which the Agency does not now have, compliance with standards of toxicity, composition, labeling, and packaging, and satisfaction of the data compensation provisions of FIFRA Section 3(c)(1)(D).

The Standard will also serve as a tool for product classification. As part of the registration of a pesticide product, EPA may classify each product for "general use" or "restricted use" [FIFRA Section 3(d)]. A pesticide is classified for "restricted use" when some special regulatory restriction is needed to ensure against unreasonable adverse effects to man or the environment. Many such risks of unreasonable adverse effects can be lessened if expressly-designed label precautions are strictly followed. Thus the special regulatory restriction for a "restricted use" pesticide is usually a requirement that it be applied only by, or under the supervision of, an applicator who has been certified by the State or Federal government as being competent to use pesticides safely, responsibly, and in accordance with label directions. A restricted-use pesticide can have other regulatory restrictions [40 CFR 162.11(c)(5)] instead of, or in addition to, the certified applicator requirement. These other regulatory restrictions may include such actions as seasonal or regional limitations on use, or a requirement for the monitoring of residue levels after use. A pesticide classified for "general use," or not classified at all, is available for use by any individual who is in compliance with State or local regulations. The Registration Standard review compares information about potential adverse effects of specific uses of the pesticide with risk criteria listed in 40 CFR 162.11(c), and thereby determines whether a product needs to be classified for "restricted use." If the Standard does classify a pesticide for "restricted use," this determination is stated in the second chapter.

Requirement to Re-register Under the Standard

FIFRA Section 3(g), as amended in 1978, directs EPA to re-register all currently registered products as expeditiously as possible. Congress also agreed that re-registration should be accomplished by the use of Registration Standards.

Each registrant of a currently registered product to which this Standard applies, and who wishes to continue to sell or distribute his product in commerce, must apply for re-regisration. His application must contain proposed labeling that complies with this Standard.

EPA will issue a notice of intent to cancel the registration of any currently registered product to which this Standard applies if the registrant fails to comply with the procedures for re-registration set forth in the Guidance Package which accompanies this Standard.

"Product Specific" Data and "Generic" Data

In the course of developing this Standard, EPA has determined the types of data needed for evaluation of the properties and effects of products to which the Standard applies, in the disciplinary areas of Product Chemistry, Environmental Fate, Toxicology, Residue Chemistry, and Ecological Effects. These determinations are based primarily on the data Guidelines proposed in 1978 (43 FR 29696, July 10, 1978, and 43 FR 37336, August 22, 1978), as applied to the use patterns of the products to which this Standard applies. Where it appeared that data from a normally applicable Guidelines requirement was actually unnecessary to evaluate these products, the Standard indicates that the requirement has been waived. On the other hand, in some cases studies not required by the Guidelines may be needed because of the particular composition or use pattern of products the Standard covers; if so, the Standard explains the Agency's reasoning. Data guidelines have not yet been proposed for the Residue Chemistry discipline, but the requirements for such data have been in effect for some time and are, the Agency believes, relatively familiar to registrants. Data which we have found are needed to evaluate the registrability of some products covered by the Standard may not be needed for the evaluation of other products, depending upon the composition, formulation type, and intended uses of the product in question. The Standard states which data requirements apply to which product categories. (See the second chapter.)

The various kinds of data normally required for registration of a pesticide product can be divided into two basic groups:

(A) data that is "product specific," i.e., data that relates only to the properties or effects of a product with a particular composition (or a group of products with closely similar composition); and

(B) "generic" data that pertains to the properties or effects of a particular ingredient, and thus is relevant to an evaluation of the risks and benefits of all products containing that ingredient (or all such products having a certain use pattern), regardless of any such product's unique composition.

The Agency requires certain "product specific" data for each product to characterize the product's particular composition and physical/chemical properties (Product Chemistry), and to characterize the product's acute toxicity (which is a function of its total composition). The applicant for registration or re-registration of any product, whether it is a manufacturing-use or end-use product, and without regard to its intended use pattern, must submit or cite enough of this kind of data to allow EPA to evaluate the product. For such purposes, "product specific" data on any product other than the applicant's is irrelevant, unless the other product is closely similar in composition to the applicant's. (Where it has been found practicable to group similar products for purposes of evaluating, with a single set of tests, all products in the group, the Standard so indicates.) "Product specific" data on the efficacy of particular end-use products is also required where the exact formulation may affect efficacy and where failure of efficacy could cause public health problems.

All other data needed to evaluate pesticide products concerns the properties or effects of a particular ingredient of products (normally a pesticidally active ingredient, but in some cases a pesticidally inactive, or "inert," ingredient). Some data in this "generic" category are required to evaluate the properties and effects of all products containing that ingredient [e.g., the acute LD-50 of the active ingredient in its technical or purer grade; see proposed 40 CFR 163.81-1(a), 43 FR 37355].

Other "generic" data are required to evaluate all products which both contain a particular ingredient and are intended for certain uses (see, e.g., proposed 40 CFR 163.82-1, 43 FR 37363, which requires subchronic oral testing of the active ingredient with respect to certain use patterns only). Where a particular data requirement is use-pattern dependent, it will apply to each end-use product which is to be labeled for that use pattern (except where such end-use product is formulated from a registered manufacturing-use product permitting such formulations) and to each manufacturing-use product with labeling that allows it to be used to make end-use products with that use pattern. Thus, for example, a subchronic oral dosing study is needed to evaluate the safety of any manufacturing-use product that legally could be used to make an end-use, food-crop pesticide. But if an end-use product's label specified it was for use only in ways that involved no food/feed exposure and no repeated human exposure, the subchronic oral dosing study would not be required to evaluate the product's safety; and if a manufacturing-use product's label states that the product is for use only in making end-use products not involving food/feed use or repeated human exposure, that subchronic oral study would not be relevant to the evaluation of the manufacturing-use product either.

If a registrant of a currently registered manufacturing-use or end-use product wishes to avoid the costs of data compensation [under FIFRA Section 3(c)(1)(D)] or data generation [under Section 3(c)(2)(B)] for "generic" data that is required only with respect to some use patterns, he may elect to delete those use patterns from his labeling at the time he re-registers his product. An applicant for registration of a new product under this Standard may similarly request approval for only certain use patterns.

Reproduced from best available copy.

Data Compensation Requirements under FIFRA 3(c)(1)(D)

Under FIFRA Section 3(c)(1)(D), an applicant for registration, re-registration, or amended registration must offer to pay compensation for certain existing data the Agency has used in developing the Registration Standard. The data for which compensation must be offered is all data which is described by all the following criteria:

(1) the data were first submitted to EPA (or to its predecessor agencies, USDA or FDA), on or after January 1, 1970;

(2) the data were submitted to EPA (or USDA or FDA) by some other applicant or registrant in support of an application for an experimental use permit, an amendment adding a new use to a registration, or for re-registration, or to support or maintain in effect an existing registration;

(3) the data are relevant to the Agency's decision to register or re-register the applicant's product under the Registration Standard, taking into account the applicant's product's composition and intended use pattern(s);

(4) the data are determined by EPA to be valid and usable in reaching regulatory conclusions; and

(5) the data are not those for which the applicant has been exempted by FIFRA Section 3(c)(2)(D) from the duty to offer to pay compensation. (This exemption applies to the "generic" data concerning the safety of an active ingredient of the applicant's product, not to "product specific" data. The exemption is available only to applicants whose product is labeled for end-uses for which the active ingredient in question is present in the applicant's product because of his use of another registered product containing that active ingredient which he purchases from another producer.)

An applicant for re-registration of an already registered product under this Standard, or for registration of a new product under this Standard, accordingly must determine which of the data used by EPA in developing the Standard must be the subject of an offer to pay compensation, and must submit with his application the appropriate statements evidencing his compliance with FIFRA Section 3(c)(1)(D).

An applicant would never be required to offer to pay for "product specific" data submitted by another firm. In many, if not in most cases, data which arespecific to another firm's product will not suffice to allow EPA to evaluate the applicant's product, that is, will not be useful to the Agency in determining whether the applicant's product is registrable. There may be cases, however, where because of close similarities between the composition of two or more products, another firm's data may suffice to allow EPA to evaluate some or all of the "product specific" aspects of the applicant's product. In such a case, the applicant may choose to cite that data instead of submitting data from tests on his own product, and if he chooses that option, he would have to comply with the offer-to-pay requirements of Section 3(C)(1)(D) for that data.

Each applicant for registration or re-registration of a manufacturing-use product, and each applicant for registration or re-registration of an end-use product, who is not exempted by FIFRA Section 3(c)(2)(D), must comply with the Section 3(c)(1)(D) requirements with respect to each item of "generic" data that relates to his product's intended uses.

A detailed description of the procedures an applicant must follow in applying for re-registration (or new registration) under this Standard is found in the Guidance Package for this Standard.

Obtaining Data to Fill "Data Gaps"; FIFRA 3(c)(2)(B)

Some of the kinds of data EPA needs for its evaluation of the properties and effects of products to which this Standard applies have never been submitted to the Agency (or, if submitted, have been found to have deficiencies rendering them inadequate for making registrability decisions) and have not been located in the published literature search that EPA conducted as part of preparing this Standard. Such instances of missing but required data are referred to in the Standard as "data gaps".

FIFRA Section 3(c)(2)(B), added to FIFRA by the Congress in 1978, authorizes EPA to require registrants to whom a data requirement applies to generate (or otherwise produce) data to fill such "gaps" and submit those data to EPA. EPA must allow a reasonably sufficient period for this to be accomplished. If a registrant fails to take appropriate and timely steps to fill the data gaps identified by a section 3(c)(2)(B) order, his product's registration may be suspended until the data are submitted. A mechanism is provided whereby two or more registrants may agree to share in the costs of producing data for which they are both responsible.

The Standard lists, in its summary second chapter, the "generic" data gaps and notes the classes of products to which these data gaps pertain. The Standard also points out that to be registrable under the Standard, a product must be supported by certain required "product specific" data. In some cases, the Agency may possess sufficient "product specific" data on one currently registered product, but may lack such data on another. Only those Standards which apply to a very small number of currently registered products will attempt to state definitively the "product specific" data gaps on a 'product by product' basis. (Although the Standard will in some cases note which data that EPA does possess would suffice to satisfy certain "product specific" data requirements for a category of products with closely similar composition characteristics.)

As part of the process of re-registering currently registered products, EPA will issue Section 3(c)(2)(B) directives requiring the registrants to take appropriate steps to fill all identified data gaps -- whether that data in question is "product specific" or "generic" — in accordance with a schedule.

Persons who wish to obtain registrations for new products under this Standard will be required to submit (or cite) sufficient "product specific" data before their applications are approved. Upon registration, they will be required under Section 3(c)(2)(B) to take appropriate steps to submit data needed to fill "generic" data gaps. (We expect they will respond to this requirement by entering into cost-sharing agreements with other registrants who previously have been told they must furnish the data.) The Guidance Package for this Standard details the steps that must be taken by registrants to comply with Section 3(c)(2)(B).

Amendments to the Standard

Reproduced from best available copy.

Applications for registration which propose uses or formulations that are not presently covered by the Standard, or which present product compositions, product chemistry data, hazard data, toxicity levels, or labeling that do not meet the requirements of the Standard, will automatically be considered by the Agency to be requests for amendments to the Standard. In response to such applications, the Agency may request additional data to support the proposed amendment to the Standard, or may deny the application for registration on the grounds that the proposed product would cause unreasonable adverse effects to the environment. In the former case, when additional data have been satisfactorily supplied, and providing that the data do not indicate the potential for unreasonable adverse effects, the Agency will then amend the Standard to cover the new registration.

Each Registration Standard is based upon all data and information available to the Agency's reviewers on a particular date prior to the publication date. This "cut-off" date is stated at the beginning of the second chapter. Any subsequent data submissions and any approved amendments will be incorporated into the Registration Standard by means of addenda, which are available for inspection at EPA in Washington, D.C., or copies of which may be requested from the Agency. When all the present "data gaps" have been filled and the submitted data have been reviewed, the Agency will revise the Registration Standard. Thereafter, when the Agency determines that the internally maintained addenda have significantly altered the conditions for registration under the Standard, the document will be updated and re-issued for publication.

While the Registration Standard discusses only the uses and hazards of products containing the designated active ingredient(s), the Agency is also concerned with the potential hazards of some inert ingredients and impurities. Independent of the development of any one Standard, the Agency has initiated the evaluation of some inert pesticide ingredients. Where the Agency has identified inert ingredients of concern in a specific product to which the Standard applies, these ingredients will be pointed out in the Guidance Package.

Chapter 2

REGULATORY POSITION

This chapter presents the Agency's decision on what Standards of product composition, toxicity, use, labeling and packaging are required for the pesticide 5-ethoxy-3(trichloromethyl)-1,2,4-thiadiazole. For ease of reading, the Agency will refer to this active ingredient as Terrazole^{R}, which is the technical producer's trade name for the product. Its use in this document does not constitute endorsement or recommendation of use by this Agency.

This decision complies with the rules and regulations (40 CFR 162) used to implement the Federal Insecticide, Fungicide and Rodenticide Act, as amended (FIFRA), and with the Agency's present regulatory policy. This Registration Standard is based upon all data and information on Terrazole available to the Agency's reviews as of December 28, 1979.

Two companies have submitted data in support of their registrations of Terrazole products: Olin Corporation of Little Rock, Arkansas and Mallinckrodt, Inc. of St. Louis, Missouri. These data may be cited by other registrants or applicants for registration, when appropriate, to support the registration(s) of their own product(s), provided they have offered and agreed to pay compensation, as required by FIFRA Sections 3(c)(1)(C) and 3(c)(2)(D).

Generic" Data Requirements

The following charts outline the data requirements of each discipline for the registration of any Terrazole product. As discussed in the preceding chapter, the "generic" data pertain to the properties or effects of the active ingredient. These studies are, therefore, relevant to the evaluation of the risks and benefits of all products containing Terrazole, regardless of the product's unique composition.

All applicants for registration or reregistration of any Terrazole product who are not exempted by FIFRA Section 3(c)(2)(D) must agree to cite available data and submit all of the information identified below as data gaps as provided for in Section 3(c)(2)(B).

A demonstration that a Terrazole product has a composition similar to a product for which the Agency already has acceptable acute toxicity data will satisfy acute toxicity data requirements for the former product. Both active and inert ingredients will be considered in making determinations of similarity. Studies such as avian reproduction, aquatic embryolarvae tests or invertebrate life-cycle tests may be required if the basic studies do not provide sufficient information to assess the hazard associated with the chemical. The need for these studies is based on specific factors derived from the intended use pattern, chemistry data, human toxicology data, residue chemistry data and basic fish and wildlife data. These studies go beyond the initial toxicity question and examine reproductive impairment and food chain magnification and other chronic effects. The specific triggers for these subsequent tests are represented in Subpart E, 43 FR 132, 29696.

TOXICOLOGY

Guidelines Section	Generic Data Requirement	Use Pattern	Do We Need Data in Column #2	Do We Have Any Data?	Will We Ask For Data In Column #2
163.81-1	Acute oral toxicity*	Ornamentals & Turf	yes	yes	no
163.81-2	Acute dermal toxicity*	Ornamentals & Turf	yes	yes	no
163.81-3	Acute inhalation toxicity*	Ornamentals & Turf	yes	yes	yes
163.81-7	Acute delayed neurotoxicity	Ornamentals & Turf	no		
163.82-1	Subchronic oral dosing	Ornamentals & Turf	yes	yes	yes
163.82-2	Subchronic 21-day dermal toxicity	Ornamentals & Turf	yes	yes	yes
163.82-3	Subchronic 90-day dermal toxicity	Ornamentals & Turf	no		
163.82-4	Subchronic inhalation toxicity	Ornamentals & Turf	no		
163.82-5	Subchronic neurotoxicity	Ornamentals & Turf	no		
163.83-1	Chronic feeding	Ornamentals & Turf	yes	yes	yes
163.83-2	Oncogenicity	Ornamentals & Turf	yes	yes	yes
163.83-3	Teratogenicity	Ornamentals & Turf	yes	yes	yes
163.83-4	Reproduction	Ornamentals & Turf	yes	yes	no
163.84-1	Mutagenicity	Ornamentals & Turf	yes	yes	yes
163.85-1	Metabolism	Ornamentals & Turf	yes	yes	no

*Required on Technical Product

ECOLOGICAL EFFECTS

Guidelines Section	Generic Data Requirement	Use Pattern	Do We Need Data in Column #2	Do We Have Any Data?	Will We Ask For Data In Column #2
163.71-1	Avian single-dose LD_{50} (a)	Ornamentals & Turf	yes	yes	no
163.71-2	Avian dietary LC_{50} (a) —wild waterfowl (a) —upland game bird (a)	Ornamentals & Turf	yes	no	yes
163.71-3	Mammalian acute toxicity (a)	Ornamentals & Turf	no		
163.71-4	Avian reproduction —wild waterfowl (a) —upland game bird (a)	Ornamentals & Turf	no		
163.72-1	Fish acute LC_{50} —cold water fish —warm water fish	Ornamentals & Turf	yes	yes	no
163.72-2	Acute toxicity to aquatic invertebrates (a)	Ornamentals & Turf	yes	no	yes
163.72-3	Acute toxicity to estuarine and marine organisms (a)	Ornamentals & Turf	no		
163.72-4	Embryolarvae and life cycle studies/fish and aquatic vertebrates (a)	Ornamentals & Turf	no		
163.72-5	Aquatic organism toxicity and residue studies (a)	Ornamentals & Turf	no		

(a) Required on technical

ENVIRONMENTAL CHEMISTRY

Guidelines Section	Generic Data Requirement	Use Pattern	Do We Need Data in Column #2	Do We Have Any Data?	Will We Ask For Data In Column #2
163.62-7 (b)	Hydrolysis	Ornamentals & Turf	yes	yes	no
163.62-7 (c)	Photodegradation	Ornamentals & Turf	yes	yes	yes
163.62-8 (b)	Aerobic soil metabolism	Ornamentals & Turf	yes	yes	yes
163.62-8 (c)	Anaerobic soil metabolism	Ornamentals & Turf	yes	yes	no
163.62-8 (d)	Anaerobic aquatic metabolism	Ornamentals & Turf	no		
163.62-8 (e)	Aerobic aquatic metabolism	Ornamentals & Turf	no		
163.62-8 (f)(2)	Effects of microbes on pesticides	Ornamentals & Turf	yes	yes	yes
163.62-8 (f)(3)	Effects of pesticides on microbes	Ornamentals & Turf	yes	yes	no
163.62-8 (g)	Activated sludge metabolism	Ornamentals & Turf	yes	yes	no
163.62-9 (b)	Leaching	Ornamentals & Turf	yes	yes	yes
163.62-9 (c)	Volatility (a)	Ornamentals & Turf	yes	no	yes
163.62-9 (d)	Adsorption/desorption	Ornamentals & Turf	yes	no	yes
163.62-9 (e)	Water dispersal	Ornamentals & Turf		no	
163.62-10 (b)	Terrestrial field dissipation (a)	Ornamentals & Turf	yes	yes	yes
163.62-10 (c)	Aquatic field dissipation (a)	Ornamentals & Turf	no		
163.62-10 (d)	Terrestrial/Aquatic (forest) ecosystem residue (a)	Ornamentals & Turf	no		
163.62-10 (e)	Specialized aquatic uses (a)	Ornamentals & Turf	no		
163.62-10 (f)	Combination and tank mixes	Ornamentals & Turf	no		
163.62-11 (b)	Rotational crops	Ornamentals & Turf	no		
163.62-11 (c)	Irrigated crops	Ornamentals & Turf	no		
163.62-11 (d)	Fish accumulation	Ornamentals & Turf	yes	yes	yes
163.62-11 (e)	Special study-aquatic non-crop (a)	Ornamentals & Turf	no		

Manufacturing-Use Terrazole

The Agency has reviewed all data available to it. Although incomplete, these data indicate that manufacturing-use Terrazole is suitable for registration because it does not meet or exceed the risk criteria leading to a Rebuttable Presumption Against Registration (Chapter 40, Section 162.11(a) of the Code of Federal Regulations). Data gaps have been identified; when these data are supplied, the Agency will again review the registration status of this compound.

A manufacturing-use Terrazole product must comply with the following standards. A manufacturing-use Terrazole product must contain Terrazole [5-ethoxy-3(trichloromethyl)-1,2,4-thiadiazole] as the sole active ingredient. Given current technical product grades and formulation methods, the Agency expects that most manufacturing-use material will range above 95% a.i. Should an applicatnt desire to register a manufacturing-use product that departs greatly from the one currently registered, that applicant should contact the Agency for specific directions on how to accomplish registration. Because Terrazole is corrosive to steel and many other metals, manufacturers of the technical material may not ship it in unlined metal containers. The acute toxicology testing on a manufacturing-use Terrazole product must demonstrate into which Toxicity Category (I through IV) the product falls for the following acute effects:

Acute Oral Toxicity;
Acute Dermal Toxicity;
Acute Inhalation Toxicity;
Primary Eye Irritation; and
Primary Dermal Irritation

The label for the currently registered manufacturing-use Terrazole product must include the following:

1. For Formulation Into End-Use Fungicide Products

The intended end-use products formulated from manufacturing-use products determines which data applicants for registration of the manufacturing-use product are required to submit or cite. The statement above obligates the manufacturer of the product to the complete battery of tests required by the Agency. This requirement could be lessened by restricting the use of the product to such categories as:

a. Domestic Use Only
b. Non-domestic Use Only
c. Non-food Use Only
d. Outdoor Use Only

2. All manufacturing-use Terrazole products must carry the following label, under the "Environmental Hazards" section:

> Do not contaminate water by cleaning of equipment or disposal of wastes.

3. All manufacturing-use Terrazole products must carry the following warning on the label:

> This product is corrosive to steel and many other metals. Do not transport or store in unlined metal containers.

4. Manufacturing-use product labels must comply with the requirements of 40 CFR 162.10 regarding label format, including placement of hazard warnings on the label, type size and color, etc.

The following charts outline the data requirements of each discipline for the registration of a manufacturing-use product. All applicants for registration or reregistration of a similar manufacturing-use product must agree to cite available data (and submit all of the information identified below as data gaps) in addition to the generic data above, in accordance with FIFRA Section 3(c)(2)(B).

A demonstration that a Terrazole product has a composition substantially similar to a product for which the Agency already has acceptable acute toxicity data will satisfy acute toxicity data requirements for the former product. However, both active and inert ingredients will be considered in making determinations for similarity.

End-Use Formulations of Terrazole

An end-use formulation of Terrazole must contain Terrazole [5-ethoxy-3(trichloromethyl)-1,2,4-thiadiazole] as the sole active ingredient. FIFRA Section 162.11(c) lists the criteria for classifying pesticides for restricted, non-domestic, or domestic use. In addition, products intended for domestic use with Toxicity Category I or II ratings for primary eye or dermal irritation must meet the criteria for child-resistant packaging [see FR 44(48): 13019-13024, March 9, 1979].

Labels for currently registered Terrazole products must include the following:

1. If emulsifiable concentrate Terrazole products contain petroleum distillates, the statement "Contains petroleum distillates" must appear on the label in close proximity to the ingredient statement. For example:

Active Ingredient
5-ethoxy-3(trichloromethyl)-1,2,4-thiadiazole .... ___%
Inert Ingredients* .... ___%
Total .... ___%
*Contains Petroleum Distillates

2. The following labeling must appear on all products which contain greater than 10% (by weight) petroleum distillates:

> "If patient is unconscious, maintain breathing and heartbeat (CPR: cardiopulomary resuscitation, if necessary). Contact your local Poison Control Center, hospital or physician immediately."

PRODUCT CHEMISTRY

Guidelines Section	Product Specific Data Requirement for Manufacturing-Use Products	Composition Characteristics	Do We Need It?	Do We Have It?
163.61-3	Product identity and disclosure of ingredients	Manufacturing-Use Product	yes	yes
163.61-4	Description of manufacturing process	Manufacturing-Use Product	yes	yes
163.61-5	Discussion on formation of unintentional ingredients	Manufacturing-Use Product	yes	yes
163.61-6	Declaration and certification of ingredient limits	Manufacturing-Use Product	yes	yes
163.61-7	Product analytical methods and data	Manufacturing-Use Product	yes	yes
163.61-8 (1)	Color	Technical	yes	yes
163.61-8 (2)	Odor	Technical	yes	yes
163.61-8 (3)	Melting point	Technical	no	
163.61-8 (4)	Solubility	Technical	yes	yes
163.61-8 (5)	Stability	Technical	yes	yes
163.61-8 (6)	Octanol/water partition coefficient	Technical	yes	yes
163.61 8 87)	Physical state	Technical and Manufacturing-Use	yes	yes
163.61.8 (8)	Density or specific gravity	Technical and Manufacturing-Use	yes	yes
163.61.8 (9)	Boiling point	Technical and Manufacturing-Use	yes	yes
163.61.8 (10)	Vapor pressure	Technical and Manufacturing-Use	yes	yes
163.61.8 (11)	pH	Technical and Manufacturing-Use	yes	yes
163.61-8 (12)	Storage stability	Manufacturing-Use	yes	yes
163.61-8 (13)	Flammability	Manufacturing-Use	yes	yes
163.61.8 (14)	Oxidizing or reducing action	Manufacturing-Use	yes	yes
163.61.8 (15)	Explosiveness	Manufacturing-Use	yes	no

Product Chemistry (continued)

Guidelines Section	Product Specific Data Requirement for Manufacturing-Use Products	Composition Characteristics	Do We Need It?	Do We Have It?
163.61-8 (16)	Miscibility	Manufacturing-Use	yes	no
163.61-8 (17)	Viscosity	Manufacturing-Use	yes	yes
163.61-8 (18)	Corrosion characteristics	Manufacturing-Use	yes	yes

TOXICOLOGY

Guidelines Section	Product Specific Data Requirement for Manufacturing-Use Products	Composition Characteristics	Do We Need It?	Do We Have It?
163.81-1	Acute oral toxicity	Manufacturing-Use Product	yes	yes
163.81-2	Acute dermal toxicity	Manufacturing-Use Product	yes	yes
163.81-3	Acute inhalation toxicity	Manufacturing-Use Product	yes	no
163.81-4	Primary eye irritation	Manufacturing-Use Product	yes	yes
163.81-5	Primary dermal irritation	Manufacturing-Use Product	yes	no
163.81-6	Dermal sensitization	Manufacturing-Use Product	yes	no

In addition, for all products which contain greater than (10% by weight) petroleum distillates, and are in Oral Toxicity Category I, the following statements must appear on the label.

> "If patient is conscious, induce vomiting (syrup of Ipecac; if not available, stimulate back of throat with finger). Never give anything by mouth to an unconscious person!"

For all products which contain greater than 10% (by weight) petroleum distillates and are in Oral Toxicity Category IV, the following statements must appear on the label:

> "Do not induce vomiting"

Products in Oral Toxicity Categories II and III will be dealt with on a case-by-case basis at the time for registration.

3. All currently registered EC Terrazole products containing 25% a.i. must carry on the label the acute toxicity hazard warnings and first aid statements required for the following Toxicity Categories (see Appendix A):

   Primary Eye Irritation - I

4. All currently registered EC Terrazole products containing 4 lbs/gal a.i. must carry on the label the acute toxicity hazard warnings and first aid statements required for the following Toxicity Categories (see Appendix A):

   Acute Dermal Toxicity - II
   Acute Oral Toxicity - III
   Primary Eye Irritation - I
   Primary Dermal Irritation - II

5. All currently registered WP/D Terrazole products containing 30% a.i. must carry on the label the acute toxicity hazard warnings and first aid statements required for the following Toxicity Category (see Appendix A).

   Acute Oral Toxicity - III

6. All currently registered granular Terrazole products containing 5% a.i. must carry on the label the acute toxicity hazard warnings and first aid statements required for the following Toxicity Categories (see Appendix A).

   Acute Oral Toxicity - IV
   Acute Dermal Toxicity - III
   Acute Inhalation Toxicity - III
   Primary Eye Irritation _ III
   Primary Dermal Irritation - IV

7. All Terrazole products must carry the following warning on the label under the "Environmental Hazards" section:

> "Do not apply directly to ponds or streams. Do not contaminate water by cleaning of equipment or disposal of wastes."

8. All labels and labeling intended for agricultural use products must bear the statement "This product must be applied in accordance with 40 CFR Part 170." Registrants may amplify the above statement on labels or labeling by stating the requirements of 40 CFR Part 170 or additions thereto, if they choose.

9. All product labels must comply with the requirements of 40 CFR 162.10 regarding label format; including placement of hazard warnings on the label, type size and color, etc.

The following charts outline the data requirements of each discipline for the registration of end-use products. All applicants for registration or reregistration of a similar end-use product must agree to cite available data and submit all of the information identified below as data gaps. For those not exempted from generic gap requirements by FIFRA Section 3(c)2)(D) the end-use data and generic data apply and must be cited or submitted in accordance with Section 3(c)2)(B).

> A demonstration that a Terrazole product has a composition similar to a product for which the Agency already has acceptable acute toxicity data will satisfy acute toxicity data requirements for the former product. Both active and inert ingredients will be considered in making determinations of similarity.

PRODUCT CHEMISTRY

Guidelines Section	Product Specific Data Requirement or End-Use Products	Composition Characteristics	Do We Need It?	Do We Have It?
163.61-3	Product identity and disclosure of ingredients	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-4	Description of manufacturing process	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-5	Discussion of formation of unintentional ingredients	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-6	Declaration and certification of ingredient limits	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-7	Product analytical methods and data	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-8(1)	Color(a)	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no

PRODUCT CHEMISTRY (Continued)

Guidelines Section	Product Specific Data Requirement for End-Use Products	Composition Characteristics	Do We Need It?	Do We Have It?
163.61-8(2)	Odor[a]	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-8(7)	Physical state[a]	30% WP/D & 35% WP	yes	yes
		25% EC	yes	yes
		4 lb/gal EC	yes	yes
		5% G	yes	yes
163.61-8(8)	Density or specific gravity[a]	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-8(9)	Boiling point[a]	30% WP/D & 35% WP	no	
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	no	
163.61-8(10)	Vapor pressure[a]	30% WP/D & 35% WP	yes	yes
		25% EC	yes	yes
		4 lb/gal EC	yes	yes
		5% G	yes	yes
163.61-8(1)	pH[a]	30% WP/D & 35% WP	yes	yes
		25% EC	yes	yes
		4 lb/gal EC	yes	yes
		5% G	yes	yes

Product Chemistry (Continued)

Guidelines Section	Product Specific Data Requirement for End-Use Products	Composition Characteristics	Do We Need It?	Do We Have It?
163.61-8(12)	Storage stability	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-8(13)	Flammability	30% WP/D & 35% WP	no	
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	no	
163.61-8(14)	Oxidizing or reducing action	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-8(15)	Explosiveness	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-8(16)	Miscibility	30% WP/D & 35% WP	no	
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G		
163.61-8(17)	Viscosity	30% WP/D & 35% WP	no	
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	no	

Product Chemistry (Continued)

Guidelines Section	Product Specific Data Requirement End-Use Products	Composition Characteristics	Do We Need It?	Do We Have It?
163.61-8(18)	Corrosion characteristics	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no
163.61-8(19)	Dielectric breakdown voltage	30% WP/D & 35% WP	no	
		25% EC	no	
		4 lb/gal EC	no	
		5% G	no	

(a) Required on both formulated and technical product.

TOXICOLOGY

Guidelines Section	Product Specific Data Requirement End-Use Products	Composition Characteristics	Do We Need It?	Do We Have It?
163.81-1	Acute oral toxicity(a)	30% WP/D & 35% WP	yes	yes
		25% EC	yes	no
		4 lb/gal EC	yes	yes
		5% G	yes	yes
163.81-2	Acute dermal toxicity(a)	30% WP/D & 35% WP	yes	yes
		25% EC	yes	no
		4 lb/gal EC	yes	yes
		5% G	yes	yes
163.81-3	Acute inhalation toxicity(a)	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	yes
163.81-4	Primary eye irritation(a)	30% WP/D & 35% WP	yes	no
		25% EC	yes	yes
		4 lb/gal EC	yes	yes
		5% G	yes	yes
163.81-5	Primary dermal irritation(a)	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	yes
		5% G	yes	yes
163.81-6	Dermal sensitization(a)	30% WP/D & 35% WP	yes	no
		25% EC	yes	no
		4 lb/gal EC	yes	no
		5% G	yes	no

ECOLOGICAL EFFECTS

Guidelines Section	Product Specific Data Requirements End-Use Products	Composition Characteristics	Do We Need It?	Do We Have It?
163.71-5(1)	Cage of pen field test[a]	30% WP/D & 35% WP	no	
		25% EC	no	
		4 lb/gal EC	no	
		5% G	no	
163.71-5(2)	Full-scale field test[a]	30% WP/D & 35% WP	no	
		25% EC	no	
		4 lb/gal EC	no	
		5% G	no	
163.72-1	Fish acute LC_{50} -rainbow[a] trout and blue gill	30% WP/D & 35% WP	no	
		25% EC	no	
		4 lb/gal EC	no	
		5% G	no	
163.72-2	Acute toxicity to aquatic[a] invertebrates	30% WP/D & 35% WP	no	
		25% EC	no	
163.72-3	Acute toxicity to estuarin and marine organisms[a]	4 lb/gal EC	no	
		5% G	no	
163.72-6(a)(1)	Short term simulated field [a] test	30% WP/D & 35% WP	no	
		25% EC	no	
		4 lb/gal EC	no	
		5% G	no	
163.72-6(a)(2)	Long-term simulated field[a] test	30% WP/D & 35% WP	no	
		25% EC	no	
		4 lb/gal EC	no	
		5% G	no	

(a) Test on typical formulated product.

Chapter 3

PRODUCT CHEMISTRY

INTRODUCTION

FIFRA 3(c)(2)(A) requires the Agency to establish guidelines for registering pesticides in the United States. The Agency requires registrants to provide quantitative data on all added ingredients, active and inert, which are equal to or greater than 0.1 percent of the product by weight.

To establish the composition of products proposed for registration, the Agency requires data and information not only on the manufacturing and formulation processes, but also a discussion on the formation of manufacturing impurities and other product ingredients, intentional and unintentional. Further, to assure that the composition of the product as marketed will not vary from the composition evaluated at the time of registration, applicants are required to submit a statement certifying upper and lower composition limits for the added ingredients, and upper limits only for some unintentional ingredients. Subpart D (43 FR, No. 132, 29696, July 10, 1978) suggests specific precision limits for ingredients based on the percentage of ingredient and the standard deviation of the analytical method.

In addition to the data on product composition, the Agency also requires data to establish the physical and chemical properties of both the pesticide active ingredient and its formulations. For example, data are needed concerning the identity and physical state of the active ingredient (e.g., melting and boiling point data, vapor pressure and solubility). Data are also required on the properties of the formulated product to establish labeling cautions (e.g., flammability, corrosivity or storage stability). The Agency uses these data to characterize each pesticide and to determine its environmental and health hazards."

TOPICAL DISCUSSION

The Topical Discussions listed below correspond to the sections in the "Proposed Guidelines for Registering Pesticides" of July 10, 1978 (43 FR, No. 132, 29696). These sections explain the minimum data the Agency requires to assess Terrazole's Product Chemistry.

Topical Discussions	Guideline Sections
Chemical Identity	163.61-3
Manufacturing Process	163.61-4
Formation of Unintentional Ingredients	163.61-5
Percentage of Active Ingredients	163.61-6
Product Analytical Methods and Data	163.61-7
Physical/Chemical Properties	163.61-8

CHEMICAL IDENTITY

The trade name "Terrazole" will be routinely used in this Standard in lieu of the chemical name, 5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole, for convenience in writing this Standard. Use of the trade name implies no endorsement of any specific product containing the active ingredient.

Other trade names are: Ethazol, Ethazole, ETMT,, Etridiazol, Etridiazole, Koban, Truban and OM2424.

The technical chemical names of Terrazole are as follows:

Chemical Name: 5-Ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole
5-Ethoxy-3-trichloromethyl-1,2,4-thiadiazole
Trichloro methylethoxy thiadiazole

Type: Fungicide

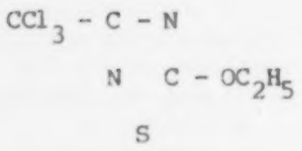
Shaughnessy # 084701

C.A.S. #: 2593-15-9

Mo. Wt: 247.5

Chemical Formula: $C_5H_5Cl_3N_2OS$

Structural Formula:



MANUFACTURING PROCESS

Details of the procedures, equipment and manufacturing conditions required for commercial production of the chemical will be discussed in Appendix A which contains confidential information protected under Section 10 of FIFRA.

According to the Farm Chemicals Handbook, 1980, Terrazole is only manufactured in the USA by Olin Chemicals, Olin Corporation, Little Rock, Arkansas.

In general, applicable U.S. Patent Nos. 3,825,581 and 3,389,338 describe the manufacture of Terrazole as follows: A mixture of trichloroacetamidine hydrochloride, trichloromethane sulfenyl chloride and methylene chloride is kept at a temperature between -4°C and 1°C while stirring and adding dropwise sodium hydroxide in water. After two hours, the methylene chloride layer is separated, washed with water then dried over sodium sulfate. After evaporation of the solvent, the residue is vacuum distilled to recover the intermediate, 3-trichloromethyl-5-chloro-1,2,4-thiadiazole. The intermediate (U.S. Patent No. 3,890,338) is dissolved in ethanol and stirred with sodium in anhydrous ethanol. After 15 minutes, the reaction mixture becomes neutral and the precipitated sodium chloride is removed by filtration. Excess ethanol is evaporated and the residue is vacuum distilled at 94.5°C and 1mm Hg to recover the product 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole. (Pesticide Process Encyclopedia, Noyes Data Corp., Park Ridge, New Jersey, 1977 GS0009-048)

FORMATION OF UNINTENTIAL INGREDIENTS

Potentially harmful impurities sometimes result during the production of pesticides. The main impurities during the production of Terrazole are 5-chloro-3-trichloromethyl-1,2,4-thiadiazole, and trichloroacetamide (Martin et al., 1977, GS0009-035). Reporting of manufacturing impurities is required by the proposed registration guidelines in the Federal Register, 43 (132) 29696 (issue of July 10, 1978), Section 163.61-7(2) and (3). The presence of manufacturing impurities depends on the nature of the reaction used. Detailed information is available to Agency personnel in Appendix A which contains confidential business information protected under Section 10 of the FIFRA.

PERCENTAGES OF ACTIVE INGREDIENT

The Registration Standard will describe the acceptable composition of the technical ingredient. This information is needed to define the acceptable ranges of active ingredient allowable in registered products, to prescribe appropriate test material concentrations in hazard evaluation testing and later, to estimate likely exposures to the active ingredient resulting from the handling or use of the products in which it is contained.

Technical Terrazole

A confidential statement of formula as submitted by Olin Chemical Corp. states that their technical grade Terrazole contains 95% 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole as the active ingredient. The remaining 5% consists of manufacturing impurities whose identifies are available to Agency personnel in Appendix B as confidential business information.

Formulated Terrazole

Formulations of Terrazole are used as fungicides against a narrow range of fungal pests (Pythium and Phytophthora species). The four types of formulations covered in this Standard are wettable powders, emulsifiable concentrates, wettable powder/dusts, and granular. Table 1.1 summarizes the uses of these formulations and Appendix B (which contains confidential business information protected under Section 10 of FIFRA) presents the ingredients of each formulation. Terrazole formulations are applied by ground equipment only including broadcast spray, irrigation systems, mechanical mixing, drench methods and granular spreaders. Typical application rates vary according to need and are shown in Table 1.1. A detailed discussion of the use of Terrazole formulations is presented in the Use Profile contained in Chapter Three.

Table 1-1. Summary of the Registered Uses of Terrazole[a]

Product Description[b]	Registered Sites	Application Rate a.i.	Method
30% WP	Turf	0.1 to 0.2 lb/1000 sq. ft.	Broadcast spray
30% WP[c]	Ryegrass Seed Treatment	1.35 to 2.1 oz/100 lb seed	Mechanical seed treater
30% WP	Ornamentals	0.8 to 0.23 lb/400 sq. ft.	Broadcast spray or through irrigation
25% EC	"	0.8 to 0.23 lb/400 sq. ft.	" " " " "
95% Technical	For formulation uses only	for manufacturing purposes	------
35%	Turf	0.1 to 0.2 lb/1000 sq. ft	Broadcast spray or through irrigation
35% WP	Ornamentals	0.8 to 0.23 lb/400 sq. ft.	Broadcast spray or through irrigation
4 lb/gal EC	Avocados	0.02 to 0.27 lb/ tree	Drenching vessel to soil
5% G	Avocados	0.02 to 0.27 lb/ tree	Granular applicator
5% G	Ornamentals	0.03 to 0.12 lb/ cu. yd. soil	Mechanical soil mixer

[a] Terrazole is a fungicide registered for use against a narrow range of fungal pests (Pythium and Phytophthora species)

[b] WP = Wettable Powder; D = Dust; EC = Emulsifiable concentrate; G = Granular
Adapted from Reference GS0009-036

[c] Wettable Powder used as a dust.

Reproduced from best available copy.

PRODUCT ANALYTICAL METHODS AND DATA

In order to ensure that products contain only those percentages of active ingredients which they properly claim to contain, it is necessary to have analytical methods to determine the concentration of active ingredients in each formulation. In addition, the commercial production of pesticide chemicals, reactions between pesticide ingredients, reactions with packaging materials, as well as degradation during the long period over which some products may be stored before use, can result in the formation of chemical impurities. Because of the potential toxicity of these impurities, analytical methods must also be provided for their assessment, both to improve the reliability of the Agency's hazard assessment and to ensure that marketed products conform to the standards of purity agreed upon by the pesticide producer.

Analytical methods for the identification and quantification of Terrazole in the manufacturing-use and formulated end-use product have been submitted. Methods for the analysis of impurities have also been submitted and are considered to be adequate. No infrared or ultraviolet spectrophotometric or mass spectra methods which may be used in the identification of Terrazole were reported.

PHYSICAL/CHEMICAL PROPERTIES

Physical/Chemical properties can serve as a means of chemical identification or as a confirmation of the reliability of other composition data.

Technical

The following Physical/Chemical properties for technical Terrazole were reported by Olin Chemical Corp. under references 00001553, 00001556, 00001760, and 00002232:

Color:	pale yellow
Odor:	musty, mildy persistent
Solubility:	practically insoluble in water. (50 ppm at 25°C) Soluble in acetone, ether, ethanol, Skellysolve^R and carbon tetrachloride

Although the Guidelines state that solubility should be determined at 20°C, the Agency feels that since Terrazole is practically insoluble in water, a 5°C temperature difference in the determination of Terrazole's solubility would not make a significant difference and does not constitute a data gap.

Freezing Point: 20-22°C

Stability: Terrazole is stable to light (including ultraviolet) and prolonged storage in sealed containers of metal or glass. Some loss will occur in polyethylene over prolonged storage of more than 3 years. Terrazole hydrolyzes with acids and bases.

Octanol/Water Partition Coefficient:

An octanol/water partition coefficient of 405 was reported at 12.5 ppm and 300 at 18.7 ppm starting concentrations. The temperature of the test was 25°C.

Physical State: Liquid

Density or Specific Gravity: 1.503 at 25°C

Boiling Point: 95°C at 1 mm mercury

Vapor Pressure: 1X10^{-4}mm Hg at 25°C
0.30mm Hg at 37.8°C
1mm Hg at 95°C
13.6mm Hg at 114.4°C

pH: 3-4 in saturated water solution

Storage Stability: The technical material is stable to prolonged storage in sealed containers. Degradation occurs after three years of storage in polyethylene containers.

Flammability: Flash point 151°C (Tagged Closed Cup Method)

Oxidizing or Reducing Action: May emit toxic fumes of chloride, oxides of sulfur and nitrogen under conditions of heat and moisture.

Explosiveness: No data reported

Miscibility: No data reported

Corrosion Characteristics: The technical material reacts with steel and many other metals, therefore, lined containers must be used. According to NACE TM-01-69, the corrosive action of Terrazole is as follows: Steel SAE 1020, 0.14; Aluminum 7075-T6, 0.09.

Formulations:

Physical/chemical properties of Terrazole formulations were not available for this Standard; however, these data are required prior to registration under this Standard.

DISCIPLINARY REVIEW

Chemistry Profile
Generic Data Gaps
Suggested Labeling

CHEMISTRY PROFILE

Terrazole contains a minimum of 95-97% of the active ingredient, 5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole. Technical Terrazole is a pale yellow to reddish brown liquid with a mildy persistent musty odor. The compound is stable when stored under normal conditions. Technical Terrazole is practically insoluble in water but very soluble in acetone, ether, ethanol, Skellysolve^{R}, and carbon tetrachloride. The specific gravity is 1.503 at 25°C and the vapor pressure is 1 mm Hg at 95°C. Because it is intended only for re-formulation into an end-use pesticide, technical Terrazole is a "manufacturing-use" product.

In order to be registrable under this Standard, a technical pesticide product containing Terrazole must have at least 95-97% concentration of active ingredient, the same or less identifiable non 5-ethoxy-3-trichloromethyl components, and physical/chemical properties comparable to those described in this chapter.

Generic Data Gaps

The following data gaps in the Product Chemistry data base are tests needed to adequately support registration for a product containing Terrazole. Following each data gap is listed the section in the Proposed Registration Guidelines of July 10, 1978 (FR 43, No. 132, 29696) which describes the type of data needed.

For Technical Terrazole and/or manufacturing-use product:

1. Explosiveness	163.61-8(c)-(15)
2. Miscibility	163.61-8(c)-(16)

For formulated end-use Terrazole:

Guidelines Section

For Emulsifiable Concentrate Terrazole:

1) Color	163.61-8(c)(1)
2) Odor	163.61-8(c)(2)
3) Density or Specific Gravity	163.61-8(c)(8)
4) Boiling Point	163.61-8(c)(9)
5) Storage Stability	163.61-8(c)(12)
6) Flammability	163.61-8(c)(13)
7) Oxidizing or Reducing Action	163.61-8(c)(14)
8) Explosiveness	163.61-8(c)(15)
9) Miscibility	163.61-8(c)(16)
10) Viscosity	163.61-8(c)(17)
11) Corrosion Characteristics	163.61-8(c)(18)

For Granular and Powder Terrazole:

1) Color....................................163.61-8(c)(1)
2) Odor.....................................163.61-8(c)(2)
3) Density or Specific Gravity..............163.61-8(c)(8)
4) Storage Stability........................163.61-8(c)(12)
5) Oxidizing or Reducing Action.............163.61-8(c)(14)
6) Explosiveness............................163.61-8(c)(15)
7) Corrosion Characteristics................163.61-8(c)(18)

Chemical Identity (163.61-3): (1) Complete identification of all impurities and reaction compounds in the technical chemical. (2) Identification of all substances appearing in the manufacturing-use and formulated products.

Manufacturing Process (163.61-4): Complete information on the present manufacturing process, including type of process, equipment and quality control measures.

Formation of Unintentional Ingredients (163.61-5): Theoretical discussion of the formation of each substance, aside from the active ingredient and intentionally added inert ingredients, that might reasonably be identified as being present in the pesticide product.

Under the Proposed Policy for Pesticides contaminated with N-nitroso compounds (45 FR, 124, 42854) applicants whose products contain at least 1 ppm N-nitroso compounds are required to perform exposure analyses as prescribed by the Agency.

Percentages of Components in Pesticide Products (163.61-6):

Declaration or certification of limits for all active and inert ingredients.

Product Analytical Methods and Data (163.61-7): Methods for analysis of formulations and submission of gas chromatography methods for the technical compound.

Suggested Labeling

Ingredient Statement: The ingredient statement will list the active ingredient, Terrazole as:

5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole.............. __%.

Physical Hazard Precautionary Labeling: Precautionary labeling may become necessary, depending on the nature of the physical/chemical properties submitted by applicants for registration in response to requirements listed in the sections of this chapter on Generic Data Gaps and Registration Requirements.

Since the technical product is corrosive to steel and other metals, the technical label must carry a warning against storage in unlined metal containers.

Bibliography

GS0009-035-- Martin, H., and C.R. Worthing, eds. 1977. Pesticide Index: Basic information on the chemicals used as active components of pesticides, 5th ed. British Corp. Protection Council, Worcestershire, England.

00001760--Olin Mathieson Chemical Corporation. 1964. Chemical and Physical Properties for Terrazole. (Unpublished study received Dec 16, 1964 under 1258-740; CDL: 119218-A)

00001556--Olin Corporation. 1966. Technical Data: Terrachlor^{R} Super X: (Terraclor^{R} + Terrazole). (Unpublished study received Jan 1, 1966? under 1258-Q; CDL: 110045-A)

00001553--Olin Corporation. 1977. Terrazole^{R} Technical Grade--Data Sheet (Unpublished study that includes data sheets A. 1-A.2, A.3, A.4, received Feb. 4, 1977 under 1258-812; CDL: 095799-A)

GS0009-036-- Pesticide Chemical Use Pattern Profile for Terrazole (084701). U.S. Environmental Protection Agency, Office of Pesticide Programs, Benefits and Field Studies Division, May 1979.

GS0009-048--Pesticide Process Encyclopedia, 1977. Noyes Data Corp. Park Ridge, New Jersey.

00002232--Schingh, J.E. 1976. Vapor Pressure Studies of Terrazole^{R} (5-Ethoxy-3-trichloromethyl-1,2,4-thiadiazole): CASR-21-76. (Unpublished study received Oct 10, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark.; CDL: 228143-

Chapter 4

ENVIRONMENTAL FATE

USE PROFILE

Use and Formulations

Terrazole^R is a soil fungicide that is registered and used against a narrow range of plant pathogenic fungi. As a single active ingredient product, it is registered in the United States for use on turf (primarily for golf courses) and ornamental crops (approximately 24 species of flowering bedding plants, 9 species of container grown plants and 10 species of tropical foliage plants); ornamental use is limited to commercial growers. Terrazole also has a state registration in California for use as a soil treatment around avocado trees. It is formulated for turf and ornamental use as a 30 and 35% wettable powder (WP), and for ornamental use only as a 25% emulsifiable concentrate (EC). The 5% Granular (G) is used to treat soil prior to seeding or transplanting of ornamentals. For use on avocados it is formulated as a 4 lb/gal EC and as a 5% granular (G). Terrazole has one use as a seed treatment; the 30% WP may be used as a dust to treat ryegrass seed.

Use Practices

For turf use, Terrazole WP formulations are applied as a broadcast spray by means of tractor mounted, or motor scooter mounted boom sprayers or vehicle mounted hand-held spray wands. The application rate is 0.1 to 0.2 lb active ingredient (a.i) in 100 gal of water per 1000 square feet (sq. ft.). Frequency of application varies with disease incidence but as many as 15 applications may be made at five to ten day intervals. Terrazole is used in all states but primarily in Southern states (Sparks, 1980, GS0009-070).

For soil treatment of bedding and tropical foliage plants the WP and EC formulations are applied through irrigation systems at 0.8 to 0.23 lb. a.i. per 400 sq. ft. or as a broadcast spray by means of a back pack or wheeled boom sprayer at the rate of 0.8 to 0.23 lb a.i. in 100 gallons of water per 400 sq. ft. Frequency of application varies with disease incidence but as many as six applications may be made at one to three month intervals. For treatment of soils prior to planting of ornamentals, Terrazole WP (as a dry powder) or 5 percent G may be incorporated into soil by means of a mechanical mixer at the rate of 0.03 to 0.12 lb a.i. per cubic yard (cu. yd.) of soil. It is used in most states but mainly in California, Florida, and Alabama (Sparks, 1980, GS0009-070).

For treatment of container grown plants (including some tropical foliage plants) the EC and the 30% WP are applied as a drench by means of sprinkling can or drench dispensing vessel at the rate of 0.05 to 0.2 lb a.i. per 100 gallons of water; 0.5 pint is used for a six inch diameter container. Frequency of application varies with disease incidence but as many as three applications may be made at two to three month intervals. Usage is primarily in California, Florida and Alabama (Sparks, 1980, GS0009-070).

For soil treatment of avocado the 5% G formulation is applied by means of a granular spreader or the 4 lb/gal EC formulation is applied by means of a drenching vessel at 0.02 to 0.27 lb a.i. per tree (1.8 to 24.3 lb per acre) to a circular area surrounding the tree. At the present time Terrazole is not extensively used in California but in the event of severe disease outbreak applications would be made at monthly intervals for nine to ten months (Geomet, 1980, GS0009-021). For treatment of ryegrass seed the 30% WP is applied at the rate of 1.35 to 21. oz. a.i. per 100 lb of seed.

Usage

It has been estimated by Geomet that on an annual basis 20,000 to 132,000 lb a.i. of Terrazole are used for treatment of from 2,570 to 2,880 acres of turf (Geomet, 1980, GS0009-021). Personal communication with Olin Corporation indicates that turf grass usage is approximately 120,000 lb (Sparks, 1980, GS0009-071). The annual usage for treatment of greater than 3,760 acres of ornamental crops has been estimated by Geomet to be approximately 98,000 lb a.i. however, calculations based on acreage estimates and application rates indicate usage at 51,000 lb (Geomet, 1980, GS0009-021). The manufacturer suggests usage at 25,000 lb for ornamentals (Sparks, 1980, GS0009-071). It has been reported that in 1979, 20 lb of Terrazole were used for treatment of avocado trees and that in the event of a widespread disease out-break 72,000 to 1,224,000 lb a.i. would be used to treat 51,200 acres (Geomet, 1980, GS0009-021). The estimated usage for avocados in 1979 was approximately 20 lb a.i. (Geomet, 1980, GS0009-020); however, communication with the manufacturer indicates that the usage greatly exceeds this figure (Sparks, 1980, GS0009-071).

Topical Discussions

The Topical Discussions listed below correspond to the sections in the "Proposed Guidelines for Registration of Pesticides" of July 10, 1978 (43 CFR No. 163). These sections explain the minimum data the Agency requires to assess Terrazole's Environmental Fate.

Topical Discussions	Guidelines Section
Physico-Chemical Transformation	163.62-7(b) and (c)
Metabolism	
Soil	163.62-8(b) and (c)
Microbial	163.62-8(f) 2 and 3
Activated Sludge	163.62-8(g)
Mobility	163.62-9(b), (c), (d), and (e)
Field Dissipation	163.62-10(b), (c), (d), and (e)
Accumulation	163.62-11(b), (c), and (d)

PHYSICO-CHEMICAL TRANSFORMATION

Hydrolysis

Hydrolysis data are usually required to support the registration of all manufacturing-use products regardless of the intended end uses of the formulated products.

Two studies relating to the hydrolysis of Terrazole were reviewed, and both were considered valid. Thomas, (1975, 00001650) determined the rate of [3-^{14}C] Terrazole hydrolysis in 0.01 M phosphate buffered solutions at pH values of 5.1, 7.1, and 8.9 and in distilled water at room temperature, in the dark. Half-life values of 82, 83, 81, and 85 days were reported under the respective experimental conditions. The acid metabolite (3-carboxy-5-ethoxy-1,2,4-thiadiazole) was reported as the only hydrolysis product. The hydrolysis of [3-^{14}C] Terrazole was also studied at 25, 35, and 45°C at specified pH values (Thomas, 1976, 00001652). The data in this study indicated that the rate of Terrazole hydrolysis increased with increasing temperature and pH (Table 1). At pH 6, half-life values of 103, 30, and 12 days were obtained at 25, 35, and 45°C, respectively. The major hydrolysis product identified was the acid metabolite.

The results of the above studies demonstrate that Terrazole is hydrolyzed in phosphate buffered solutions and in distilled water. The rate of Terrazole hydrolysis increases with increasing temperature and pH. The major hydrolysis product is 3-carboxy-5-ethoxy-1,2,4-thiadiazole.

These studies fulfill the hydrolysis data requirements in Section 163.62-7(b).

Photolysis

Photodegradation studies in water are required to support the registration of all formulated products intended for terrestrial (except greenhouse or domestic outdoors), aquatic, and terrestrial/aquatic (forest) uses. These studies are not intended to assess potential hazards that may be associated with indirect pesticide discharges into waste-water treatment systems.

In addition, studies in soil are required to support the registration of all formulated products intended for crop and terrestrial/aquatic (forest) uses.

Two studies relating to the photolysis of Terrazole were reviewed and both were judged invalid because dark controls were not employed. Thus, all data as specified in Section 163.62-7(c) are needed to determine the effect of light on Terrazole degradation.

METABOLISM

Data on metabolism are required to determine the nature and availability of pesticide residues to rotational crops and to help in the assessment of potential disposal and re-entry hazards.

Soil

Aerobic metabolism studies are required to support the registration of all formulated products intended for terrestrial uses or terrestrial/aquatic (forest) uses. Anaerobic soil metabolism studies are required to support the registration of all formulated products intended for field and vegetable crop uses.

Four studies pertaining to soil metabolism were reviewed and three were considered valid. The degradation of [3-^{14}C] Terrazole was studied after application at 1.2 ppm to Tiak sandy loam and Amy silt loam soil incubated at either 25 or 38°C (Thomas, 1976, 00001657). The concentrations of Terrazole and its degradation products, the dichloro and

Table 1. Hydrolysis half-life data for [3-^{14}C] Terrazole[a]

Temperature (C) (ppm/day)	Buffer pH	Initial Terrazole concentration (ppm)	Half-life (days)	Hydrolysis rate
25	3.0	6.23	112	0.027
	6.0	6.23	103	0.030
	9.3	6.23	109	0.028
	5.2[b]	46.0	82	0.28
	7.1[b]	43.2	83	0.24
	8.9[b]	45.0	81	0.27
	Dist. water[b]	54.0	85	0.33
35	3.0	6.23	30	0.10
	6.0	6.23	30	0.10
	9.3	6.23	20	0.15
	3.0	43.6	31.5	0.70
	6.0	40.0	30	0.65
	9.3	55.6	28.5	0.94
45	3.0	6.23	10.3	0.30
	6.0	6.23	12	0.26
	9.2	6.23	5	0.61
	3.2	40.0	9.5	2.16
	6.0	58.0	12	2.38
	9.2	59.4	7.5	3.87

a Adapted from Thomas (1976, 00001652).

b Adapted from Thomas (1975, 00001650).

acid metabolites, after 10 days of incubation under aerobic and anaerobic conditions are given in Table 2. Two other possible metabolites were CO_2 and oxalic acid (under aerobic or anaerobic conditions). Generally, after the first half-life an increase in soilbound radioactivity and decrease in Terrazole and its metabolites occur under all conditions. The half-life values of Terrazole ranged from 2 to 9.5 days under the experimental conditions described in Table 3. Metabolic pathways were postulated for aerobic and anaerobic soil metabolism of Terrazole (Figure 1). Ercegovich (1976, 00001664) confirmed that CO_2 was a metabolite of Terrazole by demonstrating that soil microorganisms released more $^{14}CO_2$ from soils treated with $[3-^{14}C]$ Terrazole than was released from similarly treated sterile soils.

The degradation of Terrazole in sandy and silt loam soils planted with green beans under greenhouse conditions was investigated (Kuchar, 1976, 00001662). No Terrazole residues remained in the silt loam soil incubated for 71 days in a greenhouse following the application of $[3-^{14}C]$-Terrazole at 2 ppm. In sandy soil, only 6 percent of the original Terrazole remained after 71 days (Table 4). At the same time, only 31 and 11 percent of the original radioactivity remained in the sandy and silt loam soils, respectively. Greater than 90 percent of the radioactivity unaccounted for by Terrazole was in the form of the dichloro metabolite. Concentrations of the acid metabolite and soilbound residues were less than 2 percent in both soils.

In summary, these studies indicate that Terrazole can be rapidly metabolized in sandy and silt loam soils under described anaerobic and aerobic conditions. The dichloro metabolite is the major metabolite formed under all described experimental conditions. The other two metabolites are CO_2 and the acid metabolite. No attempt was made to differentiate the effects of hydrolysis, photolysis, and microbial metabolism on the degradation of Terrazole. However, the formation of the dichloro metabolite and shorter half-life of Terrazole in soil than in distilled water suggest that Terrazole degradation in soil was mainly due to microbiological processes.

Anaerobic soil metabolism data requirements in Section 163.62-8(c) are fulfilled by the above studies.

Aerobic soil metabolism requirements are not fulfilled by the above studies because, according to Section 163.62-8(b), a study using soil other than sandy loam or silt loam is required to assess the fate of Terrazole in soil, and the sandy and silt loam soil studies were too short in duration.

Microbial Metabolism

Data on the effects of microbes on pesticide degradation and the effects of pesticides on microbes are required to support the registration of all formulated products intended for the following uses: terrestrial noncrop, tree fruit/nut crop, field/vegetable crop, terrestrial/aquatic (forest), and direct discharge aquatic impact.

Table 2. Degradation products of [3-^{14}C]-Terrazole applied to soil at 1.2 ppm.

Soil	Aerobic		Anaerobic	
	25°C	38°C	25°C	38°C
	% of applied Terrazole remaining after 10 days			
	Terrazole			
Sandy loam	48	51	10	0
Silt loam	48	53	25	5
	Dichloro metabolite[a]			
Sandy loam	46	15	43	13
Silt loam	31	17	48	22
	Acid metabolite[b]			
Sandy loam	--[c]	--	6	25
Silt loam	--	--	11	13

a 3-dichloromethyl-5-ethoxy-1,2,4-thiadiazole.

b 3-carboxy-5-ethoxy-1,2,4-thiadiazole.

c Not detected.

Adapted from Thomas (1976, 00001657).

Table 3. Half-lives of Terrazole in aerobic and anaerobic soils.

Metabolism	Temperature (C)	Soil	Half-life (days)
Aerobic	25	Amy silt loam	9.5
	38		6.5
	25	Tiak sandy loam	9
	38		9
Anaerobic	25	Amy silt loam	3
	38		2
	25	Tiak sandy loam	5
	38		2.5

Adapted from Thomas (1976, 00001657).

Table 4. Analysis of soils for radiolabeled Terrazole and its metabolites after incubation under greenhouse conditions.[a]

		Terrazole		Dichloro metabolite[b]		Acid metabolite[c]	radioactivity
Soil type	Total radioactivity (% of applied)	(ppm)	(% of applied)[d]	(ppm)	(% of applied)	(% of applied)	(% of applied)
Sandy	31	0.135	6.3	0.405	23.0	1.7	1
Silt loam	11	0.0	0.0	0.179	10.0	1.6	1

[a] Incubation for 71 days at 68°F; all analyses were run in duplicate and the results were averaged by the reviewer.

[b] Dichloro metabolite = 3-dichloro-5-ethoxy-1,2,4-thiadiazole.

[c] Acid metabolite = 3-carboxy-5-ethoxy-1,2,4-thiadiazole.

[d] Terrazole applied at 2 ppm.

Adapted from Kuchar (1976, 00001662).

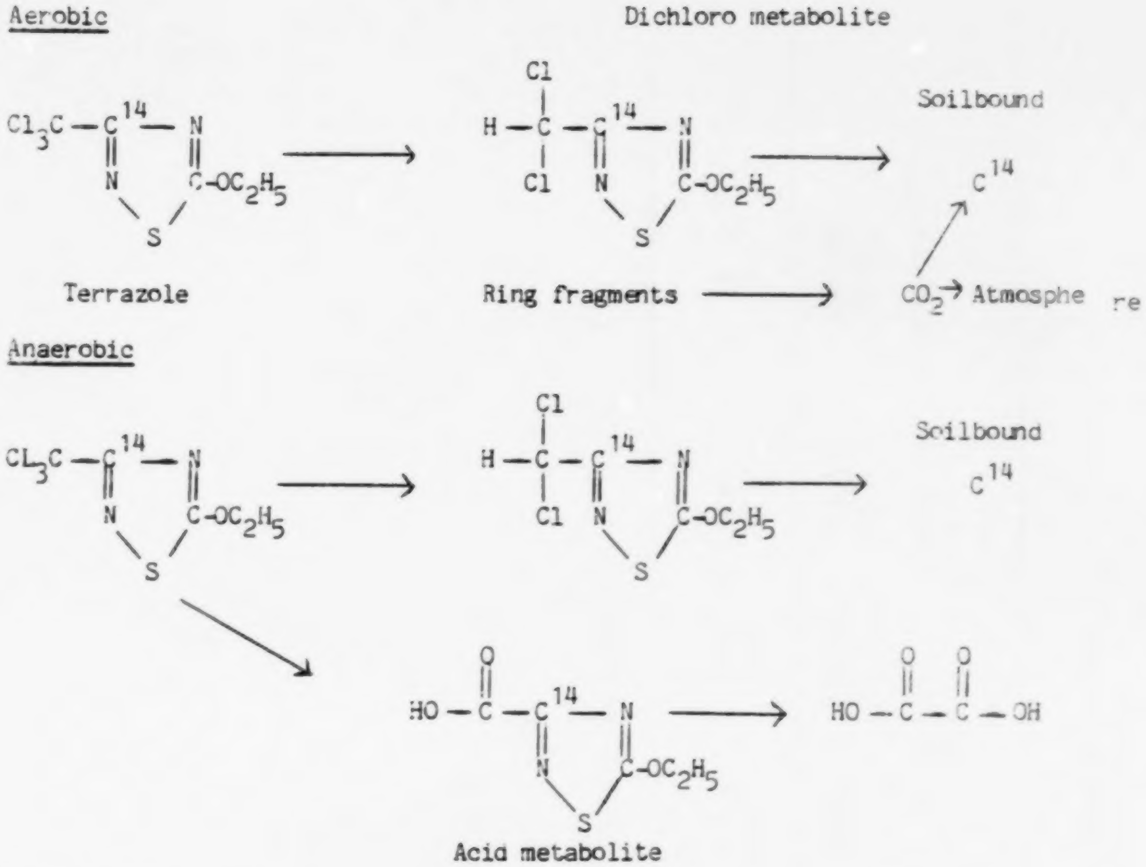

Aerobic
Dichloro metabolite
Soilbound
C^{14}
Terrazole
Ring fragments
CO_2 → Atmosphere
Anaerobic
Soilbound
C^{14}
Acid metabolite

Figure 1. Postulated metabolic pathways for aerobic and anaerobic soil metabolism of Terrazole (Thomas, 1976, 00001657).

Microbial - Effects of Microbes on Pesticides

Two studies relating to the effects of microbes on pesticides were reviewed and both were considered valid. Some preliminary information on the microbial metabolism of Terrazole is available in a report by Ercegovich (1976, 00001664), who studied the effects of [^{14}C] Terrazole on populations of bacteria and fungi in silt loam and sandy loam soils. Gradual evolution of $^{14}CO_2$ from the soil samples indicated that microbes were capable of degrading Terrazole. The highest level of $^{14}CO_2$ evolution was 6 percent of the applied radioactivity observed over a 9-week period in soil containing Terrazole at 5 ppm, whereas no $^{14}CO_2$ was evolved from sterile samples. No attempt was made to determine either the identity of the organisms that were responsible for the degradation or the degradation pathway. Kvien (1975, 00001567) also provided some preliminary evidence that microorganisms are capable of utilizing Terrazole (formulation unspecified) as a sole source of carbon. He found 6 fungal and 5 bacterial species commonly found in soil (8 and 17 tested, respectively) that were able to grow on a medium containing Terrazole as the sole carbon source. Two predominant soil organisms, *Micrococcus* and *Achromobacter*, that were capable of growing on the medium containing Terrazole were isolated from Tama silt loam soils by enrichment culture techniques.

Although the above studies are scientifically valid, they do not entirely satisfy the requirement because both the degrading organisms and the degradation pathways should be identified.

Microbial - Effects of Pesticides on Microbes

Four studies on the effects of Terrazole on microorganisms were reviewed and three were judged valid.

Kvien (1975, 00001567) demonstrated that nitrification of urea and ammonium sulfate ($(NH_4)_2SO_4$) fertilizers in soil was markedly inhibited when they were coated with Terrazole (reagent grade) or when liquid mixtures of $(NH_4)_2SO_4$ and Terrazole were used. Complete inhibition of nitrification for up to 3 weeks was observed with use of Terrazole at concentrations as low as 1-2 ppm, indicating that the level of nitrification inhibition by Terrazole was comparable to that obtained with the commercial product N-Serve (2-chloro-6-trichloromethyl pyridine).

Ercegovich (1976, 00001664) determined the effects of Terrazole on pure cultures of bacteria and fungi chosen for their prevalence and special soil functions, as well as the effects of Terrazole on microbial populations and their respiration and seven enzyme activities in silt and sandy loam soils. He found that technical Terrazole was not bactericidal at concentrations up to 30 ppm in pure cultures. Most of the 23 bacterial species tested were not profoundly affected at low concentrations (3.8-7.5 ppm) of Terrazole. Only 2 of 13 mycelial fungi were markedly inhibited by Terrazole at 100 ppm. Microorganisms that were not affected were protease, cellulase, and pectinase producers; wax and starch degraders; and nitrogen fixers and denitrifiers. In addition, Terrazole at 5 and 25 ppm in soils generally did not inhibit the growth of *in situ* populations of fungi, actinomycetes, aerobic eubacteria, anaerobes, and spore-forming bacteria. At concentrations up to 125 ppm, [3-^{14}C] Terrazole stimulated rather than inhibited CO_2 evolution. The enzyme activities in soils of phosphatase, invertase, protease, urease, and dehydrogenase were not adversely affected over a 65-day period. However, the alpha-amylase activity was inhibited for at least 8 weeks in sandy loam soil containing technical Terrazole at 25 and 125 ppm. Catalase activity was slightly inhibited for at least 21 weeks in this soil type containing technical Terrazole at 5 and 25 ppm, but not in soil containing technical Terrazole at 125 ppm.

In summary, Terrazole at field use doses markedly inhibits microbes responsible for soil nitrification; however, no other soil microbes or their function are significantly affected.

These studies fulfill the data requirements in Section 163.62-8(f)(3) pertaining to the effects of pesticides on microbes.

Activated Sludge

A laboratory study of the effects of pesticides on the wastewater treatment process is required to support the registration of all manufacturing-use products and all formulated products that are indirectly discharged into wastewater treatment systems or are used as treatments in wastewater treatment systems.

One activated sludge metabolism study was reviewed and considered valid (Iacoviello, 1979, GS0009-039). [^{14}C] Terrazole added to sludge at 8 and 80 ppm had no apparent effect on gross populations of microbes sampled 1 and 2 days after treatment. Within 47 hours, unextractable radiolabeled residues in the solids accounted for 18 and 29 percent (8 and 80 ppm levels, respectively) of the applied radioactivity in the solids was extractable. Terrazole and its dichlorometabolite accounted for only about 0.05 percent of the extractable residues; the maximum Terrazole concentration determined was 0.001 ppm 1 day after treatment at 8 ppm. The acid metabolite represented 1.8 percent of the extractable residues obtained from the solids treated at 80 ppm but was nondetectable in solids treated at 8 ppm. A total of 48-54 percent of the radioactivity was recovered from supernatant 47 hours after treatment, and the combination of Terrazole and its acid and dichlorometabolites in solution accounted for 15 percent of the Terrazole applied at 8 ppm and 43 percent of the Terrazole applied at 80 ppm. Terrazole was in the supernatant at 0.1 and 19 ppm 1 day after treatment at 8 and 80 ppm, respectively, but no detectable amounts were found during the next 24 hours. The acid metabolite was undetectable in solution 1 and 2 days after treatment with Terrazole at 8 ppm, and the rate of formation of the dichlorometabolite decreased during the second day (1st day, 1.4 ppm; 2nd day, 0.8 ppm). However, the dichlorometabolite was present at 4.7 ppm 1 day after treatment with Terrazole at 80 ppm and 17.9 ppm was formed during the next day. Similar results were obtained for the acid metabolite in the high treatment supernatant; respective values were 4 and 14.5 ppm. Only 2-3 percent of the applied radioactivity was volatilized to unidentified products during the 2-day incubation period.

In summary, this study sufficiently demonstrates that Terrazole is rapidly transformed in activated sludge, despite the rate of treatment, and that the compound has little, if any, effect on microorganisms in sludge. The study was not conducted long enough to determine the fate and impact of excessive metabolites formed from high concentrations of Terrazole added to sludge; however, it is satifactory in spite of this minor shortcoming.

MOBILITY

Data on mobility are required to determine pesticide residue movement in the environment.

Leaching

Leaching data are required to support registration of formulated products intended for terrestrial noncrop, tree fruit/nut crop, field/vegetable crop, and terrestrial/aquatic (forest) uses.

Two leaching studies were reviewed and are discussed below.

Data from soil column studies (Thomas, 1976, 00001655) indicated that [3-^{14}C] Terrazole (applied at 6.23 ug/g and eluted with aqueous 0.01 M $CaSO_4$ on a 20-cm column; three column volumes were collected) and its dichloro metabolite (formed in the column) readily leached from aged and unaged Carnasaw silt loam soils. Greater than 60 percent of the added [^{14}C]-Terrazole was found in the leachate of an unaged silt loam soil column; less than 5 percent of the added Terrazole was found in the leachate of Tiak sandy loam, Smithdale sandy loam, and Amy silt loam soils (Table 5). Comparison of leaching profiles of the aged versus the unaged soils indicated that aged soils had a greater ability to retain Terrazole and its dichloro metabolite than did unaged soils. These data indicated that a decrease in sand content and an increase in organic matter content increased the leaching of Terrazole and its dichloro metabolite which is contrary to the leaching behavior of most pesticides in soil. Consequently, further investigation into the leaching behavior of Terrazole in soil is warranted. Helling et al. (1974, 05001190) reported that technical Terrazole was immobile in Hagerstown silty clay loam, based on a soil thin-layer chromatographic (TLC) bioassay method. These data appear to contradict the results of the above study. However, the procedure of sieving the soil to 250 um removed some of the sand and changed it to a heavier textured clay loam soil; therefore, the results do not represent those for a typical Hagerstown silty clay loam soil. Nevertheless, the data do contribute to an assessment of the mobility of Terrazole in soil.

In summary, Terrazole and its dichloro metabolite are mobile in columns containing silt loam, sandy loam, loamy sand, and heavy silt loam soils, but are immobile on silt clay loam soil TLC plates.

The behavior of Terrazole in the column systems is contrary to the usual behavior of organic pesticides. Normally, less leaching occurs in soils with higher amounts of organic matter. Therefore, further assessment of the mobility of Terrazole is needed as specified in Section 163.62-9(b), in order to adequately define the movement, via leaching, of Terrazole in appropriate soils.

Volatility

Laboratory volatility studies using nonradioisotopic analytical techniques are required to support the registration of all formulated products intended for greenhouse use. No data on the volatility of Terrazole are available, thus all data as specified in Section 163.62-9(c) are needed.

Table 5. Leaching profiles of [^{14}C]-Terrazole (6.25 ug/g) from soil columns

Soil	Organic matter (%)	CEC (mg/100 g)	pH (1:1)	Radioactivity recovered from leachate (%)	Radioactivity recovered from soil of column (%)				
					0-5 cm	5-10 cm	10-15 cm	15-20 cm	20-25 cm
Tiak sandy loam	1.5	8.3	4.8	1.2	21	17	18	20	11
Amy silt loam	2.0	18	5.0	5.0	27	22	25	16	9
Smithdale sandy loam	0.9	11.5	5.7	0.9	26	20	17	16	7
Carnasaw silt loam	2.5	25.4	4.7	65	4	3	3	4	6.5
Aged Smithdale sandy loam	--[a]	--	--	1.3	66	18	9	5	1.3
Aged Carnasaw silt loam	--	--	--	23	30	7	8	7	11

[a] Not reported.

Adapted from Thomas (1976, 00001655).

Adsorption/Desorption

A laboratory study using radioisotopic or nonradioisotopic analytical techniques is required to support the registration of all formulated products intended for all terrestrial uses, terrestrial/aquatic (forest) uses, aquatic uses, and aquatic impact uses (if the pesticides are dicharged directly into the aquatic environment). One study pertaining to the adsorption/desorption of Terrazole was reviewed and considered invalid. Thus, all data specified in Section 163.62-9(d) are needed.

Water Dispersal

A field study tailored to one or more representative sites is required to support the registration of all formulated products intended for aquatic uses and aquatic impact uses (if the pesticides are discharged directly into aquatic sites).

No data on the water dispersal of Terrazole are available.

Terrazole formulations containing multiple active ingredients are used on an aquatic food crop; however, this document deals only with the single active ingredient formulations. No data on the water dispersal of Terrazole are required because the use pattern indicates that introduction of single active ingredient formulations into the aquatic environment would not occur.

FIELD DISSIPATION

A field dissipation study under actual use conditions is required to support the registration of all formulated products intended for terrestrial (except greenhouse) uses, aquatic uses, and terrestrial/aquatic (forest) uses. This document does not deal with combinations or tank mixes of Terrazole that are used on field/vegetable and aquatic food crops.

Terrestrial

Terrestrial field dissipation studies using the formulated product are required to support the registration of representative pesticide formulations intended for all terrestrial (except greenhouse) uses.

Four studies were reviewed and considered valid. Kuchar (1972, 00001763 applied a granular or dust form of Terrazole plus pentachloronitrobenzene (PCNB) to loam, clay, and sandy soils at rates of 0.125-2.5 lb Terrazole/Acre. From 2 to 3 months later, the author found no detectable levels of Terrazole or its acid metabolite (sensitivity levels of 0.005 and 0.01 ppm, respectively) except in sandy soil, in which Terrazole was found at 0.09 ppm. Kuchar (1973, 00001661) reported that no detectable Terrazole was found in any soil sample from 1 week to 3 months after application of Terrazole as a granular or emulsifiable concentrate alone or with PCNB to soil plots in Oklahoma (unspecified soil texture) at 0.5-3 lb ai/Acre. Kuchar (1976, 00001659) demonstrated that granular Terrazole (applied at rates of 1 and 10 lb ai/Acre) and its dichloro metabolite dissipated rapidly in silt clay loam and sandy loam soils. The acid metabolite dissipated at a slower rate but did not accumulate in these soils. All compounds were nondetectable by 68 days after application of Terrazole. No further information was provided on the fate of Terrazole or its metabolite.

Kuchar (1976, 00001660) also reported that granular Terrazole (applied at 1 and 10 lb ai/Acre) and its dichloro and acid metabolites dissipated to nondetectable levels by 7 weeks after application to a fine sandy loam soil. A half-life of less than 1 week for Terrazole was reported. The mechanism of dissipation was not deduced.

These studies provided preliminary data showing the rapid field dissipation of Terrazole and two of its metabolites (all compounds were nondetectable from 1 week to 3 months). If soil characteristics and soil sampling depths data were provided, the applicability of the studies would be much greater.

Data in the following use areas are needed to assess the field dissipation of Terrazole applied as a single active ingredient formulation:

- Domestic outdoor, ornamental, and turf uses - Section 163.62-10(b)(4)

Data are needed to determine the dissipation rate and the ultimate fate of the following formulations of Terrazole:

Emulsifiable concentrate	25% ai Terrazole
Wettable powder	30 and 35% ai Terrazole
Wettable powder/dust	30% ai Terrazole

ACCUMULATION

Data on accumulation are required to determine accumulation in food webs.

Fish

A laboratory study employing radioisotopic or nonradioisotopic analytical techniques is required to support the registration of all formulated products intended for terrestrial noncrop, tree fruit/nut crop, and field/vegetable crop uses; aquatic food crop and noncrop uses; terrestrial/aquatic (forest) uses; and aquatic impact (direct discharge) uses.

A single fish accumulation study was reviewed and considered valid. Iwan (1976, 0001663) investigated the possible accumulation of [^{14}C]-Terrazole residues and metabolites in the bottom-feeding channel catfish *Ictalurus punctatus* in a static system using silt loam soil. The maximum accumulation of ^{14}C radioactivity in the catfish tissue (0.3 and 0.04 ppm for high and low exposure concentrations, respectively) was reached within 3 days of exposure. On day 20, the ^{14}C radioactivity had declined to 0.09 and 0.009 ppm, respectively, for high and low exposure concentrations (0.02 and 0.002 ppm, respectively). At both exposure levels, the higher accumulation of Terrazole was found in the nonedible portions (head and viscera). The mean accumulation ratios for nonedible and edible tissue were 3.7:1 and 4.6:1 at high and low exposure concentrations, respectively. Approximately 50 percent of the ^{14}C that accumulated in the catfish tissue by day 30 of exposure was eliminated by day 30 of depuration. The mean bioaccumulation factors for high and low exposure concentrations were 9.8 (range 4.7-24.5) and 10.2 (range 4.2-21), respectively. In summary, Terrazole residues (parent plus degradates) accumulated in nontarget aquatic fish; the mean bioaccumulation factor was 10.

A fish accumulation study with a flow-through exposure system as specified in Section 163.62-11(d) is needed to fully assess the fish accumulation properties of Terrazole under conditions of continuous exposure to the parent material.

DISCIPLINARY REVIEW

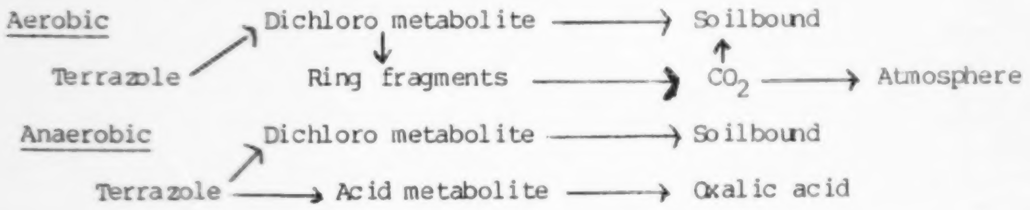
Environmental Fate Profile
Exposure Profile
Generic Data Gaps
Suggested Labeling

ENVIRONMENTAL FATE PROFILE

The environmental fate profile is designed to reflect the behavior of Terrazole in the environment. This behavior is closely associated with the use pattern of the chemical. Eventually, both Terrazole's behavior in nature and its use pattern will enable an assessment of any environmental hazards that may be associated with this chemical or any of its uses.

Available data are insufficient to fully assess the environmental fate of Terrazole. Terrazole is hydrolyzed over the environmental pH range of 5-9. The rate of Terrazole hydrolysis was found to increase with increasing temperature and pH. For example, approximately 50 percent of [^{14}C]-Terrazole was degraded over a period of 85 days in distilled water at a temperature of 25°C. The acid metabolite (3-carboxy-5-ethoxy-1,2,4-thiadiazole) was identified as the only hydrolysis product.

Radiolabeled Terrazole is rapidly metabolized in Tiak sandy and Amy silt loam soils under aerobic and anaerobic field and aerobic greenhouse conditions. The dichloro metabolite (3-dichloromethyl-5-ethoxy-1,2,4-thiadiazole) is the major metabolite; the other two metabolites are CO$_2$ and the acid metabolite. The aerobic and anaerobic soil metabolism of Terrazole appear to proceed as follows:



The half-life values for Terrazole ranged from 2 to 9.5 days under aerobic and anaerobic conditions in sandy and silt loam soils. The half-lives under aerobic conditions were two times longer than those under anaerobic conditions. Data also indicated that soilbound radioactivity increased as Terrazole and its metabolites decreased after the first half-life. In the study of soil metabolism of [3-^{14}C]-Terrazole in sandy and silt loam soils planted with green beans under greenhouse conditions, 77-89 percent of the applied radioactivity had dissipated from the soil after 71 days. Only 1 percent of the applied radioactivity was soilbound. Therefore, it is possible that observed dissipation of ^{14}C-labeled material was due to the movement of Terrazole and its metabolites away from application sites by volatilization, leaching, or translocation. Soil metabolism appears to play a major role in the degradation of Terrazole in the soil, since shorter Terrazole half-lives were observed in soils than in water and two metabolites other than the acid metabolite were obtained from soil metabolism.

Several common soil organisms (six fungal and five bacterial species) can grow on agar containing Terrazole as a sole carbon source. These are species of *Aspergillus*, *Candida*, *Geotrichum*, *Mucor*, *Rhizopus*, *Penicillium*, *Bacillus*, *Mycobacterium*, and *Micrococcus* (*Sarcina*). Through the use of a Terrazole enriched culture technique, species of *Micrococcus* and *Achromobacter* were isolated on Terrazole containing agar from Tama silt loam soils. In addition, microbes are capable of degrading [3-^{14}C] Terrazole to $^{14}CO_2$ in Smithdale sandy loam soil. The highest level of $^{14}CO_2$ evolution was 6 percent of the applied radioactivity observed over a 9-week period in soil containing Terrazole at 5 ppm. Terrazole at field use doses markedly inhibits microbes responsible for soil nitrification; however, no other soil microbes or their functions will be significantly affected.

Data from soil column leaching studies indicated that [^{14}C]Terrazole and its dichloro metabolites readily leached from aged and unaged Carnasaw silt loam soil with 2.5 percent organic matter, but little leaching occurred in Tiak sandy loam, Smithdale sandy loam, and Amy silt loam soils having organic matter contents of 2 percent or less. Data also showed that aged Terrazole-treated soils appeared to have a greater binding ability than unaged treated soils. Thus more Terrazole residues become soilbound and less leaching occurs as the soils age. Due to its relatively slow hydrolysis and its leaching characteristics, Terrazole residues may present potential hazards in the aquatic environment or with respect to ground water contamination. Additional studies as outlined under Data Gaps will provide information that will help to define the potential and extent of groundwater contamination. However, monitoring studies may be required to adequately define the potential hazard. The chemical is persistent and does pose potential accumulation problems in ground water.

Field dissipation studies confirmed the potential for notable movement of Terrazole in the soil. No Terrazole residues were detected in sandy loam, loam, or sandy soils 5 weeks after treatment with Terrazole in granular or emulsifiable concentrate formulations at rates up to 10 lb ai/Acre. The dichloro and acid metabolites dissipated to negligible levels by 8 weeks after application. The overall half-life of Terrazole is approximately 1 to 2 weeks.

The available data do not indicate significant long-term accumulation of Terrazole in fish. Terrazole residues accumulated in catfish exposed to aged [3-^{14}C] Terrazole in a static system. The maximum accumulation was reached within 3 days of exposure. By day 20 of exposure to the compound at high and low concentrations (0.02 ad 0.002 ppm, respectively) in water, residue levels had declined to 0.09 and 0.009 ppm ^{14}C, respectively, and stayed at these levels to the end of the exposure period. Approximately 50 percent of the ^{14}C that accumulated in the catfish edible tissue by day 30 of exposure was eliminated by day 30 of depuration. The mean bioaccumulation factor for radioactive residues was 10.

When Terrazole is added to sludge there is no effect on gross microbial populations, and the compound is rapidly degraded to trace levels. The acid and dichloro metabolites can accumulate in solution to 40 percent of the applied Terrazole. At low treatment levels (e.g., 8 ppm) the acid metabolite is undetectable for 2 days after treatment and the rate of formation of the dichloro metabolite decreases about 50 percent from the first to the second day post-treatment; the total amount representing about 25 percent applied Terrazole. Only 2-3 percent of the applied Terrazole is volatilized after 2 days in sludge. About 50 percent of the applied amount becomes associated with the solids, half of which is unextractable.

In summary, although data deficiencies exist which prevent forming a comprehensive profile of the fate of Terrazole in the environment, the available information indicates that Terrazole is hydrolyzed slowly under environmental conditions and is metabolized rather rapidly in soil by several soil/fungi and bacteria. The overall half-life value in soil is less than 10 days. Major degradation products are its acid metabolite (3-carboxy-5-ethoxy-1,2,4-thiadiazole) and its dichloro metabolite (3-dichloro-methyl-5-ethoxy-1,2,4-thiadiazole). The other product is CO_2 under aerobic conditions. Terrazole at field use doses has no adverse effects on soil microbes or their functions except for nitrification. Terrazole and its dichloro metabolite can leach through most types of soils. Terrazole and its metabolites dissipate rapidly in soil by means of hydrolysis, microbial degradation, and leaching. In addition, once the initial half-life is reached, soilbound residues rapidly accumulate. The potential for long-term accumulation of Terrazole and its metabolites in catfish appears low and is further reduced by depuration.

EXPOSURE PROFILE

Introduction

Single active ingredient formulations of Terrazole are registered for control of *Pythium* on turf (35% WP; 30% WP/D), *Pythium and Phytophthora* on ornamentals (30% WP; 35% WP; 25% EC, 5% G) on avocados (California only, 4 lb/gal EC; 5% G). Application to turf (primarily golf course greens) is by boom sprayers or from 400-500 gallon tanks with hand-held spray wands. Control of soil fungi on ornamentals is mainly through irrigation systems, by soil drench, and to a lesser extent, by dry soil incorporation. Terrazole appplication to avocado trees is by soil drench with the EC formulation or by surface application and flushing with the granular formulation.

All Formulations

Single active ingredient formulations of Terrazole are not applied aerially, and are therefore not expected to result in direct contamination hazards (via spray drift) to humans, livestock, or wildlife outside the application sites. The potential for exposure via spray drift is further minimized by the use of boom type sprayers (as opposed to air blast machines) which direct the spray downward. The greatest potential for direct exposure is to the mixers and applicators of these formulations, but no quantitative data are available to estimate the degree of such exposure. The low vapor pressure of the manufacturing-use product(1×10^{-4} mm Hg at 25 C) suggests a limited potential for exposure by inhalation of volatilized Terrazole.

The relatively slow hydrolysis of Terrazole ($t_{1/2}$ at about 103 days at pH 6 and 25°C), and the apparent leaching of Terrazole and its dichloro metoblite, indicate a potential for groundwater contamination and exposure of aquatic organisms. An octanol/water partition coefficient of 405 (at 12.5 ppm in water at 25°C) suggests the possibility of bioaccumulation, but bioassay data do not show long-term accumulation of Terrazole in the channel catfish, *Ictalurus punctatus*. Under static test conditions, a mean bioaccumulation factor of approximately 10 was reported for this fish, with maximum accumulation occurring within 3 days of exposure. Exposure to terrestrial organisms is expected to be minimized by rapid field dissipation.

Emulsifiable Concentrate Formulations

Emulsifiable concentrates of Terrazole are registered for control of *Phytophthora* and *Pythium* on ornamentals, and *Phytophthora* on avocados. The potential for dermal and ocular exposure is recognized from splashing which may occur during dilution and tank-mix operations. When soil drench is accomplished by irrigation, exposure to Terrazole can occur when the EC containers are opened and the injector tubing is inserted. Dermal exposure can also occur during handling of treated plants, but there is no information as to the extent of such exposure.

Wettable Powder and Wettable Powder/Dust Formulations

The greatest human exposure resulting from the use of Terrazole is expected in persons involved in the mixing and application of formulations registered for use on turf (35% WP; 30% WP/D). This is due to the widespread use of these formulations, especially for control of *Pythium* on golf courses, and because applications are repeated up to six times per year. Respiratory exposure, from "puff" back during opening and pouring of these formulations may represent the greatest exposure potential. Dermal or inhalation exposure to persons (golfers and groundskeepers) following turf application is considered small.

The use of the 35% WP as a dry soil mix for control of *Phytophthora* and *Pythium* on ornamentals can result in dermal exposure when workers handle treated soil. Such exposure would be limited, however, by the use of gloves, and because this use of Terrazole is a minor method of application in large grower operations.

The use of WP and WP/D formulations should not result in exposure to wildlife or livestock during application, due to the use of directional sprayers which reduce the potential for spray drift. The potential for human exposure via contamination of drinking water cannot be ruled out.

Granular Formulations

The granular formulation is used in very small quantities to control root rot of avocados and as a dry soil mix to control damping-off root and stem rot in outdoor plantings of ornamental and nursery stock. These uses will allow primarily dermal exposure. Dermal contact can be essentially prevented by the use of gloves for workers while handling the fungicide and the treated soil. Under those conditions, exposure to the granular formulation would be insignificant.

A 5% granular formulation of Terrazole is registered for control of *Pythium* and *Phytophthora* on ornamentals, and *Phytophthora* on avocados (California only).

GENERIC DATA GAPS

The following are data gaps in the Environmental Fate data base. These date are needed to adequately support registration of Terrazole under this Standard.

	Guideline Sections
For Manufacturing-Use Terrazole:	
(1) Photolysis	163.62-7(c)
(2) Soil Metabolism	
- Aerobic	163.62-8(f)(2)
(3) Microbial Metabolism	
- Effect of microbes on pesticides	163.62-8(f)(2)
(4) Mobility	
- Leaching	163.62-9(b)
- Volatility	163.62-9(d)
(5) Field Dissipation	
- Terrestrial: household and noncrop use for the following formulations: 25% ai EC; 30 and 35% ai WP; 30% ai D; 5% G	163.62-10(b)(4)
(6) Accumulation	
- Fish: using a flow-through exposure system	163.62-11(d)

Suggested Labeling

There are no environmental fate requirements for manufacturing-use Terrazole labels and no label restrictions for end-use products with Terrazole as the sole active ingredient.

BIBLIOGRAPHY

00001664--Ercegovich, C.D. 1976. Effects of 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole (Terrazole) on microorganisms and biochemical processes in soil: Report No. E-1/1/76 (O). (Unpublished study received Oct. 20, 1976, under 1258-812; prepared by PA. State Univ., University Park, Pesticide Research Laboratory; sumbitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL: 228143-AD.

GS0009-020--Geomet Technologies, Inc., Compilation of Data Related to Exposure to Terrazole, Geomet Technologies, Inc., Rockville, MD, May 14, 1980a.

GS0009-021--Geomet Technologies, Inc., Use Data for Exposure Analysis of Terrazole, Geomet Technologies, Inc., Rockville, MD, July 17, 1980b.

05001190--Helling, C.S., D.G. Dennison, and D.D. Kaufman, 1974. Fungicide movement in soil. Phytopath 64(8): 1091-1100.

GS0009-039-- Iacoviello, S.A. 1979. Activated sludge test for Terrazole 3-^{14}C (3-trichloromethyl-5-ethoxy-1,2,4-thiadiazole). (Olin Corp. report CASR-14-79, prepared Apr. 12, 1979 by Olin Research Center, Analytical Department, New Haven, CN) (CDL: 238774)

00001663--Iwan, G.R. 1976. Olin--^{14}C Terrazole channel catfish *(Ictalurus punctatus* Rafinesque), static bioaccumulation study. (Unpublished study received Oct. 20, 1976, under 1258-812; prepared by Union Carbide Corp, Aquatic Environmental Sciences; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL: 228143-AB.)

00001763--Kuchar, E.J. 1972. Residues of Terrachlor, Terrazole and metabolites in soil: CASR-5-72. (Unpublished study including letter dated Oct. 12, 1972, from R.F. Philpitt to P.C. Williams, received Oct. 17, 1972, under 1258-Q; submitted by Olin Corp., New Haven , CN CDL: 120359-A).

00001661--Kuchar, E.J. 1973. Residues of Terrachlor and Terrazole in soil --1972 studies: CASR-19-73. (Unpublished study received Oct. 20, 1976, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark CDL: 228143-X.)

00001659--Kuchar, E.J. 1976. Field soil dissipation studies concerned with Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole: CASR-6-76. (Unpublished study received Oct. 20, 1978, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL: 228142-S.)

00001660--Kuchar, E.J. 1976. Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole) greenhouse studies in soil: CASR-24-76. (Unpublished study received Oct. 20, 1976, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL: 228143-Y).

00001567--Kvien, C. 1975. Nitrification inhibition in soils by Terrazole. Master's thesis, Southern Illinois University, Department of Plant and Soil Science. (Unpublished study including report no. 3067, received Feb. 4, 1977, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL-095799-J.)

GS0009-070--Sparks, D., Sales Manager, Crop Protection Chemicals, Olin Corp., Little Rock, Ark, personal communication to E.N. Pelletier, BFSD, EPA, Washington, D.C. March 31, 1980a.

GS0009-071--Sparks, D., Sales Manager, Crop Protection Chemicals, Olin Corp., Little Rock, Ark, personal communication to E.N. Pelletier, BFSD, EPA, Washington, D.C., Aug. 11, 1980b.

00001650--Thomas, R.J. 1975. Analytical investigations concerned with the rate of hydrolysis of Terrazole-C-14: CASR-7-75. (Unpublished study received Oct. 20, 1976, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL:228143-H.)

00001652--Thomas, R.J. 1975. Analytical investigations concerned with the rate of hydrolysis of Terrazole-C-14: CASR-7-75. Supplement #1. (Unpublished study received Oct. 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL:228143-J.)

00001657--Thomas, R.J. 1976. Laboratory soil metabolism studies concerned with Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole): CASR-7-76. (Unpublished study received Oct. 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL:228143-Q.)

00001655--Thomas, R.J. 1976. Laboratory soil leaching studies concerned with Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole): CASR-4-76. (Unpublished study received Oct. 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL:228143-M.)

Chapter 5

TOXICOLOGY

TOPICAL DISCUSSIONS

The Topical Discussions listed below correspond to the number of the section in the Proposed Guidelines (43 FR, No. 163, 37336) which explains the minimum data that the Agency usually requires in order to assess a pesticide's Toxicology. Where no section number is listed a minimum requirement has not been set for such information.

	Guidelines Section(2)
Metabolism and Pharmacodynamics	163.85-1
Acute Effects and Neurotoxicity	163.81-, -2, -3, and -7
Subchronic Effects and Neurotoxicity	163.82-1, -2 -4, -5,
Sensitization	163.81-6
Chronic Effects	163.83-1
Oncogenicity	163.83-2
Mutagenicity	163.84-1, -2, -3, and -4
Teratology	163.83-3
Reproductive Effects	163.83-4
Emergency Treatment	

METABOLISM AND PHARMACODYNAMICS

Metabolism studies are required with a single dose of analytically pure, radioactive Terrazole.

Technical

A series of studies of Terrazole metabolism in Dutch rabbits, Wistar rats, and mongrel dogs was conducted by McKennis et al. (1970, 00001599). Two forms of radiolabeled Terrazole were administered at doses of 0.87 to 6 mg/kg in single doses with or without pretreatment at 5.75 mg Terrazole per kg body weight. Doses were administered in olive oil and the ^{14}C label was on the thiadiazole ring (carbon 3) or in the ethoxy group. Urine and expired air were analyzed for radioactivity and were also analyzed chemically to determine the amount of the administered dose excreted and the chemical nature of metabolites over various periods of time following treatment.

All three species metabolize Terrazole to a water soluble carboxylic acid (3-carboxy-5-ethoxy-1,2,4-thiadiazole) which is rapidly excreted in the urine. Rats eliminated 69 percent of the administered dose in 72 hours while rabbits excreted approximately 43 percent of a similar dose (5.75 mg/kg) in the same amount of time. A small fraction of the radioactivity from ^{14}C ethoxy labeled Terrazole was eliminated in expired air which indicates that de-ethylation of Terrazole or its carboxylic acid metabolite does occur. Pretreatment of animals with daily doses of 5.75 mg Terrazole per kg body weight for 3 to 18 days prior to administration of labeled Terrazole had little effect on excretion rates.

Four male and four female mongrel dogs were administered a single oral dose of 32-54 mg/kg Olin 2424 as a 5 percent solution in corn oil (Olin, 1965, 00001577). Blood, urine and fecal samples were collected from six animals at intervals up to 72 hours after dosing, and residues of Terrazole in various organs were determined at necropsy (72 hours) in two of six dogs. Blood was collected from two other dogs 2 and 4 hours after dosing, and tissue residues were determined at necropsy (4 hours). Terrazole residues found in blood at various intervals ranged from 1 to 2.4 ppm 2 hours after treatment, and 0.8 to 1.3 ppm 6 hours after treatment. Terrazole levels were measured in various organs from one dog of each sex both 4 and 72 hours after dosing. The highest "apparent residues" (no control samples) were found in fat 4 hours after treatment and ranged from 24 to 28 ppm. Fat samples were not analyzed at the 72-hour necropsy. No Terrazole was detected in any of the fecal samples, and only very low levels were present in urine samples.

Kuchar (1970a, 00001597) administered CM52424 (more than 95% Terrazole) at levels of 0, 10, 100, and 1,000 ppm in the diet to groups of four male and four female beagle dogs for periods of up to 2 years. Blood and urine samples were taken at 1,3, and 12 months. The dogs were sacrificed after 12 or 24 months.

Blood levels of animals at the 1,000 ppm level were in the 0.25 to 0.55 ppm range at the end of both 1 and 12 months. However, at the end of 3 months, the average blood level in these animals was only 0.068 ppm (range 0.046 to 0.90). The recovery of CM52424 from blood averaged about 85 percent.

Urinary levels of CM52424 showed no relationship with the amount of test compound ingested. No CM52424 was detected at the 0 ppm and 10 ppm feeding levels throughout the first 12 months. (No measurements were available for the 2nd year). The highest levels were recorded in a female at the 100-ppm dose level after 6 months (0.042 ppm). The percentage of recovery of CM52424 from the urine averaged about 80 percent.

The highest concentration of CM52424 was present in fat tissue. The average tissue levels for controls and animals receiving 1,000 ppm are presented in Table 3-1. There was no chromatographic evidence of a metabolite of CM52424 in any of the tissues.

Kuchar (1970b, 00001601) conducted in vitro studies to determine if 3-carboxy-5-ethoxy-1,2,4-thiadiazole and 3-carboxy-5-hydroxy-1,2,4-thiadiazole are formed when 8.9 mg of Terrazole is added to 20 ml of simulated gastric juice at pH 2.0, 5.5 or 9.5. The quantities of these compounds formed (based on the amount of Terrazole reacted) showed that 3-carboxylic acid is the only product found after 4 hours (see Table 3-2). The 3-carboxy-5-hydroxy product was found to account for 2 percent of the Terrazole reacted after 24 hours.

TABLE 3-1--Tissue Residues in Dogs Given Diets Containing Terrazole

Tissue type (% recovery)	OM52424			
	12 months		24 months	
Kidney (85%)				
0	Not detected (M)			
1,000	0.60 (M)	0.59 (F)	0.23 (M)	0.50 (F)
Brain (90%)				
0	Not detected		Not detected	
1,000	0.30 (M)	0.22 (F)	0.46 (M)	0.37 (F)
Liver (77%)				
0	Not detected		Not detected	
1,000	0.02 (M)	0.02 (F)	Not detected	
Muscle (84%)				
0	-		Not detected	
1,000	-		4.66 (M)	0.64 (F)
Fat (85%)				
0	Not detected		Not detected	
1,000	21.6 (M)	12.4 (F)	17.7 (M)	9.8 (M)
Spleen				
0	Not detected		-	
1,000	0.14 (M)	0.10 (F)	-	
Heart (89%)				
0	Not detected		-	
1,000 (total)	1.8 (M)	1.7 (F)	-	
1,000 (fat)	7.3 (M)	6.3 (F)		

TABLE 3-2--Terrazole Reactions in Simulated Gastric Juice at 37°C based on mg Terrazole consumed)

ph	Hours	% Terrazole reacted	3-carboxy
2.0	4	3	26
		13	4
5.5	4	11	5
		6	7
9.5	4	6	10
		11	2
2.0	24	13	7
5.5	24	1	65

This study indicates that Terrazole is susceptible to chemical breakdown in gastric juice. The trichloromethyl group of Terrazole is cleaved in acid or base at 37°C to yield the 3-carboxy acid product. The enol ether group is also cleaved within 24 hours at pH 2.0 and 37°C, leading to the 3-carboxy-5-hydroxy product. These polar acid products derived from Terrazole are probably less readily absorbed from the gut.

Terrazole (purity unspecified) was found to be an inhibitor of the microsomal enzyme system in a study by Dalvi and Howell (1977, 05004729). Liver microsomes were prepared from mice 24 hours after administration of a single intraperitoneal dose of 2.0 moles/kg (495 mg/kg) of Terrazole.

Concentrations of cytochrome p-450 in microsomes from livers of these mice were decreased to one-third of control values. Both benzyphetamine demethylase and aniline hydroxylase activities were also markedly decreased. Pre-incubation of Terrazole (with and without NADPH) with cytochrome P-450 from mice with pretreated phenobarbitol produced decreased cytochrome P-450 only when both Terrazole and NADPH were present in the incubation medium, indicating that Terrazole may require metabolism to produce a toxic effect in the liver.

The effect of Terrazole on NADPH stimulated lipid peroxidase activity in phenobarbitol induced mouse liver microsomes was investigated. Mixtures of NADPH and the mouse liver microsomes were incubated with EDTA (an inhibitor of this type of lipid peroxidase activity), with Terrazole (1 mM in DMSO), or with nothing added. Activity was determined by the amount of malonaldehyde formed. Results showed that EDTA completely inhibited lipid peroxidase activity and Terrazole inhibited activity by 30 to 40 percent when compared to the NADPH-microsome mixture alone.

In summary, a single water-soluble urinary metabolite of Terrazole (3-carboxy-5-ethoxy-1,2,4-thiadiazole) has been detected in the rabbit, rat, and dog (McKennis et al. 1970, 00001599). Terrazole is rapidly metabolized in rat and rabbit to this mono-acid and de-ethylated metabolites and eliminated in urine at a rate of 69% in rats and 43% in rabbits within 72 hours. The highest Terrazole residues in the tissue of the dog, after both acute and subchronic dosing, were found in fat (Olin 1965, 00001547; Kuchar 1970a, 00001597). No metabolites were identified in tissues analyzed by gas chromatography (electron capture detector). In the gut, the trichloromethyl group breaks down to give the mono-acid, and the enol ether group degrades to the 3-carboxy-5-hydroxy product. Terrazole or a metabolite inhibits the mitochondrial oxidative metabolism in mouse liver. These data adequately characterize Terrazole's metabolism.

ACUTE EFFECTS AND NEUROTOXICITY

Oral Toxicity

The minimum data requirements for testing acute oral toxicity are as follows: one test (LD_{50}) for the technical formulation and one test for each end-use formulation, preferably using the laboratory rat.

Technical

In male rats, the acute oral LD_{50} of technical Terrazole (95.2% active ingredient) as a 10 percent solution in corn oil was estimated to be 1,077 ±

78 mg/kg (Larson and Borzelleca, 1967, 00001555). The only reported clinical sign of toxicity before death was severe depression. Perianal staining (but no frank diarrhea) was observed in most of the animals dosed. No obvious pathological changes were seen on necropsy. The data place technical Terrazole in Toxicity Category III (See Appendix) for acute oral toxicity.

The following two studies represent supplemental information on Terrazole's toxicity. In male albino rabbits the LD_{50} of technical Terrazole (95.2% active ingredient) dissolved in corn oil was 779 ± 532 mg/kg (Larson and Borzelleca, 1970, 00001792). Evidence of diarrhea was observed. Yellow livers were observed at necropsy in several animals that had received 1,000 or 3,000 mg/kg of Terrazole.

In female mice, the LD_{50} for technical Terrazole (purity unspecified) at a concentration of 10 percent in a 0.25% agar emulsion was 2,000 ± 290 mg/kg (Miller, 1961, 00001586). Four of the 50 mice had impaired motor activity on the day of treatment, and weight loss was noted during the 10-day observation period. However, dose levels, necropsies, number of deaths, and statistical methods were not reported.

Wettable Powder Formulations

One study is available on a wettable powder formulation containing 30% Terrazole (Moulton, 1970a, 00001592). The acute oral LD_{50} in male and female rats (when this formulation was administered in an aqueous solution) was 4.70 g/kg. No adverse clinical signs were observed in animals receiving the lowest dose (1.26 g/kg). Signs of toxicity in animals receiving the higher dose levels included malaise, ataxia, body tremors, diarrhea, pallor, piloerection, lacrimation, weakness, arched back, inactivity, belligerence, and hypersensitivity to touch. The severity of the clinical signs was related to the dose. The major proportion (number unspecified) of survivors appeared normal by the end of the 14-day observation period. Necropsy of the animals that died during the study showed that the majority (number unspecified) had moderate-to-severe congestion of the gastrointestinal tract, adrenals, lungs, and kidneys, and speckled livers. One to five hemorrhages were observed in the stomach linings of four of these animals. Necropsy of the survivors revealed liver damage in five animals, thickening of the stomach wall in two animals, and pitted kidney surface in two animals. The data indicate that this formulation should be placed in Category III (See Appendix) for acute oral toxicity.

No data exist concerning the acute oral toxicity of the wettable powder formulation containing 35% Terrazole. However, since the confidential statement of formulation indicates that it is similar in composition to the 30% WP product the acute oral LD_{50} is expected to be similar and therefore further testing is not required.

Emulsifiable Concentrate Formulations

One study is available for the 4 lbs/gallon emulsifiable concentrate formulation of Terrazole (Palanker and Goldhamer, 1973, 00001828). In male and female rats, the acute oral LD_{50} of this formulation was 1.3 ml/kg with a 95 percent confidence interval of 0.8 to 2.1 ml/kg. Depression was noted in most animals during the first 4 days of observation; survivors appeared normal by the 7th day and remained so through the end of the study. Necropsies were not performed. These results place the 4 lbs/gallon formulation in Category III with respect to its acute oral toxicity.

No acute oral toxicity studies were available for the 25% emulsifiable concentrate formulation.

Wettable Powder/Dust and Granular Formulations

There are no acute oral toxicity data on the 30% wettable powder/dust products containing Terrazole. However, since the confidential statement of formulation indicates that this product has a similar composition to the wettable powder formulations, its acute oral LD_{50} is expected to be similar and therefore further testing is not required.

In an acute oral toxicity study, (Nham, Dan, et a, 1977, GS0009-034) rats were given various doses of the 5% granular as a 40 percent (w/v) corn oil suspension. The results indicated that the acute oral LD_{50} for these animals was greater than 15,380 mg/kg since only one male died at this dose and no other mortalities were reported. Toxic signs observed during the 9 day observation period included hypoactivity, diarrhea, muscular weakness, nasal discharge, emaciation and high stance. Necropsy of the animal that died during the test revealed depletion of body fat, 3 hemorrhaged areas on the pyloric stomach lining, pale and mottled liver, purple testes and slight post mortem autolysis. Survivors showed no gross pathological alterations. The 5% granular formulation is in Category IV with respect to its acute oral toxicity.

Dermal Toxicity

The minimum data requirement for acute dermal toxicity (LD_{50}) is one test for the technical formulation and one test for each end-use formulation, preferably using the albino rabbit.

Technical

In male albino rabbits (strain unspecified), the acute dermal LD_{50} of technical Terrazole was found to be 1,366 ± 544 mg/kg (Larson and Borzelleca, 1964a, 00002227). The skin was not erythematous after the first day. Deaths were preceded by signs suggesting depression of the central nervous system. No histopathological examinations were conducted, but the gross necropsies were essentially negative. The data indicate that this formulation should be placed in Category II (See Appendix) with respect to its acute dermal toxicity.

Wettable Powder Formulations

Moulton (1970b, 00001593) studied the acute dermal toxicity of a wettable powder formulation containing 30% Terrazole. He determined the minimum Lethal Dose of the formulation to be 2 g/kg for male and female New Zealand albino rabbits, when applied as a 50% aqueous solution. Dermal signs included slight-to-moderate erythema and slight-to-severe edema, with three of the eight treated animals (sex and dose unspecified) showing scattered yellowish lesions at the site of application 24-48 hours after exposure. Systemic signs of toxicity were weakness, anorexia, hypothermia, and muscular uncoordination of the limbs. At the highest dose level, 4 g/kg; both animals died; one died at the next lowest level, 2 g/kg; the rest of the treated animals survived.

Necropsies revealed liver damage in animals that died during the treatment period; no pathologic changes were observed in the survivors, except a small sized liver in one animal. Three of the five survivors also sufferred moderate weight loss over the 4-day observation period. These results are sufficient to place this formulation in Category II (See Appendix) since the LD_{50} is expected to be approximately 2g/kg.

There are no data concerning the acute dermal toxicity of the wettable powder formulation containing 35% Terrazole. However, since the confidential statement of formulation indicates that it is similar in composition to the 30% WP product the acute dermal LD_{50} is expected to be similar and therefore further testing is not required.

Emulsifiable Concentrate Formulations

The only acute dermal toxicity study on an emulsifiable concentrate formulation was performed by Duhamel and Paa (1978, 00001831) with 4 lb/gallon EC Terrazole. In young adult New Zealand albino rabbits, the acute dermal LD_{50} of this formulation, when administered undiluted, was 1.3 g/kg with a 95% confidence interval of 0.8-2.1 g/kg. Skin irritation ranged from moderate at lower dose levels to severe at higher levels. At the lower levels the animals had pale erythema, mild edema, and moderate desquamation. At the higher levels, the animals had well-defined erythema, severe edema, second-degree burns, and escharosis. At middle dose levels and above, brief initial hyperactivity was followed by hypoactivity that persisted until death, or, for 1-5 days in survivors. Also, at high doses the majority of the animals suffered muscular weakness from the first day. At the highest doses muscular weakness was accompanied by ataxia and tremors. Animals in the middle dose groups showed analgesia and mydriasis from day 1 until death, or until day 5 in the case of the only survivor. For the animals that died, 12 or 18 necropsies were obscured by autolysis; of the 6 remaining animals, some were reported to have discolored livers or kidneys. Three of these six animals had red or hemorrhagic lungs, two had enlarged gall bladders, and one showed a depletion of body fat. No lesions were reported in any of the animals sacrificed at the end of the study. The data indicate that this formulation is in Toxicity Category II (See Appendix) with respect to its acute dermal toxicity.

No acute dermal toxicity studies were available for the 25 % emulsifiable concentrate formulations.

Wettable Powder/Dust and Granular Formulations

There are no acute dermal toxicity data on the 30% wettable powder/dust product containing Terrazole. However, since the confidential statement of formulation indicates that this product has a similar composition to the wettable powder formulations its acute dermal LD_{50} is expected to be similar and therefore further testing is not required and this formulaltion is placed in Toxicity Category II for acute dermal toxicity.

An acute dermal toxicity study with the 5% Granular formulation indicated that the dermal LD_{50} is greater than 16,000 mg/kg when the 5% G was administered to New Zealand albino rabbits. In this study two male and two female rabbits were administered 16,000 mg/kg of the 5% G under an occlusive wrap (one half of the animals had abraded skin and one half had non-abraded skin). No mortalities or pharmacotoxic symptoms were observed. Slight edema and barely perceptible erythema were reported at 24 hours and slight desquamation of the skin was noted at 7 and 14 days. At necropsy no gross pathological alterations were seen. The granular formulation has been placed in Toxicity Category III for acute dermal toxicity.

Inhalation

The minimum data requirement for testing acute inhalation toxicity (LC_{50}) is one test for the technical formulation and one test for each end-use formulation that produces a respirable vapor, or that have 20 percent or more of their aerodynamic equivalent composed of particles not larger than 10 microns. Use of the laboratory rat is preferred.

Technical

The only study is one by Carson (1964, 00001591), reporting no deaths among a group of 10 FDRL albino rats exposed to Olin 2424 at a level of 200 mg/liter of air (length of exposure not specified). No details were provided on the methods used in generating the test atmosphere, aerosol size distribution, or sex of the animal. This study is not completely reported and therefore does not describe inhaltion toxicity adequately.

Wettable Powder Formulations

There are no data on acute inhalation toxicity on the two wettable powder formulations. An acute inhalation study is required with either one of these products or with the wettable powder/dust formulation.

Emulsifiable Concentrate Formulation

Drier et al. (1978, 0000182) exposed male and female rats for 4 hours to a nominal concentration of 60.40 mg/liter of Terrazole Fungicide 4 lb/gallon Emulsifiable. During exposure, several of the animals exhibited signs of ataxia, paralysis, hypoactivity, and squinting. Subsequently, three of five males and one of five females died, all within 4 days. Gross pathologic examination revealed diffuse redness throughout the lungs of the animals that died. Because of the brief description of the methods used in generating the test atmosphere and the lack of information on particle size, this study is judged to be insufficient to satisfy the Proposed Guidelines Requirements. No acute inhalation toxicity studies were available for the 25% emulsifiable concentrate formulations.

Wettable Powder/Dust and Granular Formulations

No acute inhalation toxicity data exist for the 30% wettable powder/dust formulation (see testing requirements under the wettable powder formulations).

An acute dust inhalation study (Weaver, Grade and Sullivan, 1977, GS009-035) indicated that the LC_{50} for Terrazole 5G is greater than 2.33 mg/l. In this study, five male and five female rats were given whole body exposure to a gravimetrically determined concentration of 2.33 mg/l of the dust for four hours. Microscopic determination of the particle size distribution revealed that 20.9 percent were 6 to 10 microns and 0.8 percent were 1 to 5 microns in size. No mortalities were observed and the only toxic sign reported was a red nasal discharge in six of the animals observed at 60 minutes post exposure and persisting for up to 17 hours in some of the animals. Necropsy revealed no abnormal gross pathological alterations. The formulation has been placed in Toxicity Category III with respect to its acute inhalation toxicity.

Eye Irritation

The minimum data requirement for primary eye irritation is one test on the technical formulation and one test for each end-use formulation product, preferrably using the Albino rabbit.

Technical

Technical Terrazole was not irritating to the eyes of rabbits (Larson and Borzelleca, 1964, 00001590). Instillation of either Olin 2424-9-0 or a 50 percent aqueous suspension of Olin 2424-9-0 produced no damage to the cornea or iris. The blood vessels of the conjunctivae showed slight dilatation but not enough for a Draize score of 1. No testing was conducted on eyes washed after treatment. The results place technical Terrazole in Toxicity Category IV, indicating a low potential for eye irritation.

Wettable Powder Formulations

There are no data for primary eye irritation for the two wettable powder formulations. A primary eye irritation study is required with either one of these products or with the wettable powder/dust formulation.

Emulsifiable Concentrate Formulations

Scibor (1978, 00001830) found that Terrazole Fungicide 4 lb/gallon Emulsifiable caused persistent irritation when administered undiluted into the conjuctival sac of rabbits. Damage to the conjunctiva (redness, chemosis, hemorrhaging, and chemical burns), iris (congestion, swelling, folds above normal), and the cornea (opacity) was noted. The reaction to Terrazole treatment in the unwashed eyes was more severe than in the washed eyes. The maximum mean irritation scores were 23.4/110 for washed eyes and 34.8/110 for unwashed eyes. In both washed and unwashed eyes, the signs were most severe at the 24-hour examination and then gradually subsided. However, after 14 days, damage to the conjunctiva and cornea was still apparent. These results place this formulation of Terrazole into Toxicity Category I (See Appendix) indicating a considerable potential for eye damage as the result of corneal opacities.

In another study conducted by Scientific Associates, Inc (1979, GS0009-031) it was shown that an Experimental 25 EC produced corneal opacity and conjunctival irritation that persisted for at least seven days in three out of nine treated eyes. In this study, the undiluted chemical was placed into one eye of each of nine New Zealand white rabbits. The treated eyes of 3 of the rabbits were washed with lukewarm tap water. All eyes were washed with isotonic saline after the 24 hour examination. The 25 EC has been placed in Toxicity Category I for primary eye irritation because of corneal opacities resulting from experimental treatment of animals.

Wettable Powder/Dust and Granular Formulations

No data on primary eye irritation exist for the 30% wettable powder/dust formulation (see testing requirements under the wettable powder formulations).

In a primary eye irritation study, (Nham, Dan, et al 1977, GS0009-034) the 5 G instilled into the conjunctival sac of the right eye of 9 rabbits. No corneal opacity or iris irritation was observed in any of the treated eyes. Conjunctival irritation was observed in all of the treated eyes. In the washed eyes (3/9) the irritation cleared by 48 hours and in the unwashed eyes (6/9) it cleared by day 7. The chemical has been placed in Toxicity Category III because of its moderate primary eye irritation.

Dermal Irritation

The minimum data requirement for primary dermal irritation is one test on the technical formulation and one test on each end-use formulation product, preferably using the albino rabbit.

Technical

Millstein (1961, 00001593) reported on acute dermal toxicity after testing Terrazole (purity unspecified) on rabbits (strain unspecified) at 200 mg/kg and at 750 mg/kg. Only one rabbit of 3 at the highest dose died. This death was not considered to be compound-related. No necropsies were performed. All animals had slight erythema, which abated within 72 hours at the lower dose and was accompanied by dry skin at the higher dose. This information is not sufficient to assign a Toxicity Category.

Wettable Powder Formulations

There are no data on primary dermal irritation for either of the two wettable powder formulations. A primary dermal irritation study is required with the wettable powder/dust formulation.

Emulsifiable Concentrate Formulations

New Zealand albino rabbits received a single application of 0.5 ml of Terrazole 4 lb/gallon Emulsifiable Concentrate on each of two areas of skin, one intact and one abraded (Palanker and Goldhammer, 1973, 00001828). The material caused slight erythema at both sites that disappeared in 75 percent of the cases within 72 hours of application. These results place the emulsifiable concentrate in Toxicity Category IV, indicating a very low potential for dermal irritation.

No primary dermal irritation studies were available for the 25% emulsifiable concentrate formulations.

Wettable Powder/Dust and Granular Formulations

There are no data on primary dermal irritation for the 30% wettable powder formulation (see testing requirements under the wettable powder formulations).

A study (Nham, Dan, et al, 1977, GS0009-034) showed that the 5% G is minimally irritating when 500 mg are applied to the abraded and intact skin of six New Zealand albino rabbits. In this study rabbits exhibited minimally irritating erythema that cleared at 72 hours; no edema was observed. The formulation has been placed in Toxicity Category IV because of its low primary dermal irritation.

Dermal Sensitization

The minimum data requirement for dermal sensitization is an intradermal test for technical formulations and for each end-use formualtion, preferably using the guinea pig.

A dermal sensitization study with Terrazole technical was conducted (Anon, 1978, GS0009-030). Validation of this study (SPRD 4/16/80) indicated that there was a significant amount of missing data, therefore, the study cannot be considered to fulfill the minimum data requirements. Dermal sensitization studies must be performed on Terrazole technical and all of its formulations.

Acute Delayed Neurotoxicity

The minimum data requirement for acute delayed neurotoxicity is one test for the technical formulation using the adult hen. These data are required if the active ingredient or any of its metabolites, degradation products, or impurities cause esterase depression, or are structurally related to a substance that induces delayed neurotoxicity.

Terrazole does not meet these criteria, so data on acute delayed neurotoxicity are not needed. The signs of neurological effects reported in many of the acute toxicity studies occurred shortly before death and within a few days of treatment. They are not characteristic of delayed neurotoxicity.

SUBCHRONIC EFFECTS AND NEUROTOXICITY

Subchronic Oral Toxicity

The minimum data requirement for subchronic oral toxicity is one test on the technical formulation in two mammalian species, preferably the rat and the dog.

Technical

In a range-finding study, male and female albino rats were given Olin 2424 (95.3% Terrazole active ingredient) in the diet at 0, 78, 312, 1,250, 5,000, or 20,000 ppm for 3 weeks (Medical College of Virginia, 1963, 00001589). At the two highest dose levels, the rate of growth for rats of both sexes was markedly depressed. With the exception of one male rat at the 5,000 ppm level, all rats at these two dose levels died during the 3-week study period. The growth rate of male rats at the 1,250 ppm level also was depressed. No other differences from the controls in survival or rate of growth were observed at the three lower dose levels. Both sexes showed dose-related increases in liver-to-body weight ratios. No significant compound-related differences were observed in hematological parameters at 2 weeks.

In a subchronic study, male and female Wistar rats were fed diets containing 0, 78, 156, 312, 625, or 1,250 ppm (active ingredient) of OM-2424 for a period of 3 months (Larson, 1963a, 00001600). Throughout the study, a moderate depression was observed in the rate of growth for animals of both sexes at the highest dose level. At the lower levels, no reduction in body weight was noted until the final month, when the average body weight of animals receiving 625 ppm was slightly depressed. No dose-related differences in survival, food consumption, hematologic parameters, or urinary proteins and reducing substances were observed. Dose-related increases were observed in the liver-to-body weight and kidney-to-body weight ratios in both male and female rats.

Histopathologic examination revealed no lesions that could be related to the ingestion of OM-2424. Although there are statistically significant increases in the kidney-to-body weight ratios at four out of five dose levels (including the low dose), a NOEL is considered to be 312 ppm since there were no effects on clinical chemistry or histopathology in the liver or kidneys of treated animals to confirm toxic effects which were suggested by organ-to-body weight ratios.

Subchronic oral toxicity studies have been conducted on OM-2424 with dogs.

A range-finding study was conducted with four male or female mongrel dogs (alternating sexes). The dogs were fed diets containing 312, 1,250, 5,000 or 20,000 ppm (active ingredient) of OM-2424 for 4 weeks (Larson, 1963c, 00001588). The female dog at the 5,000-ppm level died during the 4th week. All dogs receiving the three highest doses lost weight during the study, but their food consumption was also reduced. Focal periportal fatty changes were observed in the 20,000 ppm male.

Groups of two male and two female beagle dogs were provided diets containing 0, 100, 400, or 1,600 ppm (active ingredient) OM-2424 for 3 months (Larson, 1963b, 00001650). No deaths occurred during the study. Three of the four dogs at the 1,600 ppm level lost weight during the study; this loss of weight was attributed to a reduction in food consumption. No dose-related differences in hematology, urine analysis, liver function, or clinical signs were observed during the 13-week test. Spleen-to-body weight ratios were depressed at all three treatment levels. Congestion of the spleen was observed in one low-dose male dog. Liver-to-body weight ratios were elevated in high-dose dogs.

In a 2-year study (Larson and Borzelleca, 1968a, 00001697), male and female beagle dogs were fed Olin 2424 (95.3% Terrazole) in the diet at 0, 10, 100, and 1,000 ppm (active ingredient). The body weights of the high-dose dogs were depressed throughout the study, particularly during the first 13 weeks, but food consumption at this level was also reduced. During the first year, all blood chemistry values were normal. However, during the second year, serum levels of alkaline phosphatase and cholinesterase were significantly elevated in dogs of both sexes at 1,000 ppm. Bromosulphthalein retention times were increased for males at 1,000 ppm at 18 and 24 months. At 24 months, significant increases were seen in serum level of glutamic-oxaloacetic transaminase in 100-ppm females. Hematologic and urinalysis determinations revealed no treatment-related effects. Liver weights and liver-to-body weight ratios were significantly elevated in male and female dogs at the 1,000 ppm level. Male dogs at the 1,000 ppm level also exhibited increased kidney-to-body weight ratios at 24 months. Histopathologic examination revealed cholestatic hepatosis with secondary bile nephrosis in 1,000-ppm treated males and females. This effect is not considered to be compound related because an increase in transaminase was not observed in the 100 ppm gap and no abnormal histopathology was observed in their liver. Administration of Terrazole did not cause any other histopathological lesions. Therefore, the "no-observed effect level" (NOEL) for this study is considered to be 10o ppm.

21-Day Dermal Toxicity

The minimum data for the subchronic 21-day dermal toxicity requirement is one study for the technical formulation, preferably using the albino rat.

Technical

Groups of six male and six female albino rabbits received application of technical Terrazole (Olin 2424-9-0) 5 days a week for 3 weeks on abraded skin at doses of 0, 94, 188, 375, or 750 mg/kg/day (Larson and Borzelleca, 1965, 00001571). It was not stated if measures were taken to prevent ingestion of the test substance, so the observed effects cannot definitely be attributed to dermal absorption. The dose levels of 375 and 750 mg/kg/day caused 100 percent mortality; 188 mg/kg/day caused 25 percent mortality; no death was reported at the 94-mg/kg/day level. Weight losses were seen in the three high-dose groups. Unspecified toxic signs suggestive of central nervous system depression were observed before death. Erythema of the treated areas of skin was observed at all dose levels after one or two applications; the skin became hard and crustlike after three to five applications. Hematological parameters (hematocrit, hemoglobin, and white blood cell counts) were lower for treated rabbits of both sexes than for controls. Gross and histopathological examinations showed dose-related effects for lesions of the liver, kidney, myocardium, and skin.

Inhalation

The minimum data requirement for subchronic inhalation toxicity is one test for the technical formulation preferably using the albino rabbit. This test is not required for Terrazole since repeated inhalation exposure is not expected for humans.

Neurotoxicity

The minimum data requirement for subchronic neurotoxicity is one test for the technical formulation, preferably using the adult hen. A subchronic neurotoxicity evaluation is not required because Terrazole does not depress esterase activity, and it is not structurally related to a compound that induces neuropathy or delayed neurotoxicity.

CHRONIC EFFECTS

Feeding

The minimum data requirement for chronic toxicity is one test for the technical formulation preferably using the laboratory rat.

Technical

Male and female CD-strain rats were fed diets containing 0, 10, 80, or 640 ppm of Olin 2424 (95.3% Terrazole) for 2 years (Larson, 1968, 00001696). Except for a slight early retardation in growth in males at the 640 ppm level, no treatment-related differences in survival, growth rate, or food consumption were noted between treated and control groups. At the end of 6 months, the following organ-to-body weight ratios were significantly elevated above that of untreated controls: kidney and liver for 640 ppm treated females and spleen and testes for 640 ppm treated males. After 2 years, liver-to-body weight ratios in the 640 ppm treated males were significantly increased. Except for a dose-related increase in white blood cell counts in female rats at 6 months, no abnormalities were detected by hematological or clinical biochemistry, urinalysis, and gross pathologic evaluations. In male rats, the incidences of glomerulonephrosis and testicular atrophy were seen to increase with increasing dose levels of Terrazole but statistical significance was not noted. The NOEL for this study was 80 ppm. The small number of animals undergoing complete histopathological examination limit the value of this study for assessing the chronic toxicity and oncogenic potential of Terrazole.

ONCOGENICITY

The minimum data requirement for oncogenicity is one test in each of two mammalian species the for technical formulation. The rat and mouse are preferred test species. The rat study discussed under "Technical" above is not sufficient to satisfy this requirement, and there is no available long-term feeding study in mice.

MUTAGENICITY

The following studies represent only the minimum requirements for data on the potential heritable effects of Terrazole.

1. A mammalian in-vitro point mutation test.
2. A sensitive sub-mammalian point mutation test (Bacteria, fungi, insect).
3. A primary DNA damage test (i.e., sister chromatid exchange or unscheduled DNA synthesis).
4. A mammalian in-vitro cytogenetics test. If this test suggests a positive result, a dominant lethal or heritable translocation test may be required.

After results from these test systems and other toxicology disciplines have been considered, additional testing may be required to further characterize or quantify the potential genetic risks.

Although the Agency's mutagenic testing requirements are not final, the standards for these tests should be based on the principles set forth therein (43 FR, No. 163). Protocols and choices of test systems should be accompanied by a scientific rationale. Substitutions of test systems for those listed above will be considered after discussion with the Agency.

These requirements should be considered as an interim guide and not final Agency policy. However, the Agency does consider the above testing scheme to be a reasonable minimum requirement.

Bacterial assays were conducted with technical grade Terrazole in Salmonella typhimurium strains TA 100, TA 1535, TA 98, TA 1537, TA 1538, and TA 1978 as well as Escherichia coli strains WP2, WP2VVRA, WP67, WP6, M611, CM571, W3110, and P3478 (Ercegovich and Kashid, 1977, GS0009-032). The assays detect reverse mutations resulting from base pair substitution or frameshift events. These assays also detect effects on DNA repair (in E. coli strains W3110 and P3478). Effects of liver microsomal activation have also been investigated (Ercegovich and Kashid, 1977, GS0009-032). Terrazole had no mutagenic activity in these bacterial systems although the doses were sufficiently high to produce toxicity in some of the strains. (High doses ranged from 1000 to 5000 mg per disc).

This study satisfies the requirements for sub-mammalian point mutation test as outlined in Section 163.84-1(b)(2)(i)(A).

TERATOGENICITY

The minimum data requirement for teratogenicity testing is two mammalian species using the technical formulation.

In a study conducted by Knickerbocker and Re (1979, GS0009-033) groups of at least 15 pregnant Dutch-belted rabbits were given daily doses of 0, 1.5, 5, 15 or 45 mg Terrazole in corn oil per kg body weight. Doses were administered by gavage on days 6 through 18 of gestation. A 2 mg/kg dose of 6-aminonicotinamide was given by gavage to a group of pregnant rabbits as the positive control. No effects on material body weights or the incidence of soft tissue and skeletal anomalies in fetuses from the 1.7, 5, or 15 mg/kg/day group were seen when they were compared with the untreated control group. However, the highest dose caused three deaths or abortions in the 17 rabbits tested. The mean maternal body weight for the 45 mg/kg does was also decreased below that for untreated dams at gestation day 18 (see table III). The number of live fetuses per doe and the percentage of does with resorptions was increased above that for the lower dose and untreated control groups. The highest dose also reduced fetal weights and increased the number of litters with anomalies. The anomalies observed included missing sternebrae, tail defects, crossed hind legs, and open eyes. These effects cannot conclusively be attributed to Terrazole since maternal toxicity was also indicated by the three deaths and weight loss in the does given the highest dose. This experiment does not distinguish between fetal effects caused by Terrazole and fetal effects resulting from poor health of the dams in the high dose group. The NOEL in this study is considered to be 15 mg/kg/day.

TABLE III-3 Summary of Results of the Rabbit Teratology Study

Finding	Control	45 mg/kg/day group
Mean maternal body weight	2.38 ± 0.06 kg	2.12 ± 0.09 kg
Live fetuses/does	5.3	3.5
Percentage of does with resorptions	29.4%	57.1%
Mean fetal weights	41.7 g	32.8 g
Number of litters with anomalies/total number of litters		
Skeletal		
Tail defects	0/17	5/9
Missing sternebrae	0/17	3/9
Soft tissue		
Hind legs crossed	0/17	2/9
Eyes open	0/17	2/9

REPRODUCTIVE EFFECTS

The minimum data requirement for reproductive effects is testing in one mammalian species, preferably the laboratory rat, using the technical formulation and lasting for at least two generations.

Technical

For Terrazole, a three-generation reproduction study with two litters per generation was conducted on rats (Larson and Borzelleca, 1968b, 00001698). Technical Terrazole (Olin, 2424) was administered in the diet at concentrations of 0, 10, 80, or 640 ppm. At the high dose, reductions in weanling weights and adult weights were seen in both males and females at the time of the first and second matings. The no-observed effect level with respect to pup weight decreases is considered to be 80 ppm.

EMERGENCY TREATMENT

No information on the prevention and treatment of Terrazole intoxication is available.

DISCIPLINARY REVIEW

Toxicology Profile
Toxicity Hazard Assessment
Generic Data Gaps
Suggested Labeling

TOXICOLOGY PROFILE

Manufacturing-Use Terrazole

Sufficient data are available to show that Terrazole has moderate acute oral toxicity. The oral LD_{50} values are 1,077 (±78) mg/kg/body weight in male rats, 779 (±532) mg/kg in male rabbits, and 2,000 (±290) mg/kg in female mice. The latter two values were reported without sufficient detail to completely evaluate their adequacy. Signs of toxicity observed were depression in rats receiving relatively high doses, diarrhea and yellow livers in rabbits receiving doses greater than the LD_{50}, and weight loss in mice 10 days after dosing.

The data are sufficient to demonstrate a relatively high degree of acute dermal toxicity. The acute dermal LD_{50} value is 1,366 (±544) mg/kg. Signs of depression were reported.

Insufficient data are available to completely assess the acute inhalation toxicity. However, rats exposed to air containing 200 mg/liter for an unknown period of time showed no mortality.

There are sufficient data indicating that Terrazole causes little primary eye irritation.

There are insufficient data to completely assess the primary skin irritation potential of Terrazole. However, skin of rabbits exposed to 200 mg/kg body weight for 24 hours had erythema while that of rabbits exposed to 750 mg/kg for 24 hours had erythema with dryness. These signs disappeared within 72 hours after exposure. There are no data available on skin sensitization.

There is insufficient data on the subchronic toxicity since there is only one full study in dogs. The no-observed effect level with respect to effects on blood chemistry was 10 ppm in the diet of dogs for two years. Another study conducted in rats was stated to be a range finding study and cannot be used in the evaluation of subchronic toxicity.

A 21-day dermal toxicity study in rabbits did not demonstrate a no-effect level. There was no indication that steps were taken to prevent the ingestion of the test material, so that the observed results cannot be definitely attributed to dermal absorption.

One study in rats reported a no-effect level of 80 ppm in the diet for two years. However, since a less than adequate number of animals were examined microscopically, the study's value in evaluating chronic toxicity and oncogenicity is limited and additional testing is required.

A three generation reproduction study in rats demonstrated a no effect-level of 80 ppm with respect to pup body weight decreases.

A teratogenicity study in rabbits showed that 15 mg/kg/day had no fetotoxic or teratogenic effects. At 45 mg/kg, maternal toxicity was noted along with fetal effects. A teratology study in a second species (preferably rats) is required.

Terrazole had no mutagenic activity in two species of bacteria with or without microsomal activation.

Sufficient data is available to satisfy the mutagenicity requirements for a bacterial assay as stated in Sections 163.84-1(b)(2)(i)(A). Studies done in various strains of *Salmonella typhimarium* and *Escherichia coli* , showed that Terrazole technical is not mutagenic. However, mammalian *in vitro* point mutation, *in vitro* cytogenics and heritable translocation or dominant lethal, and primary DNA damage assays are needed. The last requirement can be satisfied by sister chromatid exchange or unscheduled DNA synthesis studies.

There are sufficient data on the metabolism of Terrazole in the rat, rabbit and dog. The primary metabolite is 3-carboxy-5-ethoxy-1,2,4-thiadiazole which is excreted in the urine. In the rat an average of 69 percent of the 5.75 mg/kg dose was excreted in 72 hours. For the rabbit this amount was 43 percent for the same dose. The greatest amount of residues were found in the fat of dogs (no metabolites were identified in tissues).

Wettable Powder Formulations

There are sufficient data on the acute oral toxicity of the 30% Wettable Powder formulation to show that it has moderate toxicity. The LD_{50} value in male and female rats is 4.70 g/kg body weight. Signs of toxicity in animals receiving the highest doses included ataxia, tremors, diarrhea, pallor, piloerection, lacrimation, arched back, inactivity, and hypersensitivity to touch. Survivors appeared normal by the end of the 14-day observation period. Congestion of the gastrointestinal tract, adrenals, and kidneys was noted. Liver damage and thickening of the stomach wall was seen in survivors.

Sufficient data are available on the acute dermal toxicity of the wettable powder formulations. The minimum lethal dose for albino rabbits is 2.0 g/kg. Signs of dermal toxicity included erythema, edema. Other signs included weakness, anorexia, hypothermia, and lack of muscular coordination in the limbs. Both animals died after 4 g/kg was applied to their skin while one of the two died after receiving an application of 2 g/kg.

There are no data on the inhalation toxicity, primary eye irritation primary dermal irritation, and dermal sensitization for both the 30 and 35% WP. Since the confidential statement of formulation indicates that these two products and the wettable powder/dust formulation have similar compositions and thus are expected to have similar acute toxicities and irritation potentials, testing of at least one of the products in the above outlined studies will fulfill the data requirement.

Emsulfiable Concentrate Formulations

Sufficient data are available to show that the acute oral LD_{50} for the 4 lb/gallon emulsifiable concentrate containing 48 percent Terrazole is 1.3 ml/kg/body/weight (0.08 to 2.1, 95% confidence limits.) Depression is the only sign of toxicity reported.

There are sufficient data to show that the acute dermal LD_{50} of Terrazole 4 lb/gallon EC is 1.3 g/kg/body weight (95% confidence limits are 0.8 to 2.1 g/kg). Skin irritation in this study ranged from moderate at the lower levels (0.27 to 0.7 g/kg) to severe at the higher dose levels (0.6 to 16 g/kg).

Insufficient data are available to completely assess the acute inhalation toxicity of the 4 lb/gallon emulsifiable concentrate. A concentration of 60.50 mg/liter of air when breathed by male and female rats for four hours caused ataxia, paralysis, hypoactivity and squinting. Three of five males and one of five females died within 4 days after exposure. A complete evaluation cannot be made without further details regarding the methods and results in this test.

There are sufficient data to classify the 4 lb/gal emulsifiable concentrate as a severe eye irritant. It caused redness, chemosis, and hemorrhaging of the conjunctiva; congestion, swelling and greater than normal folding in the iris; and corneal opacity in the eyes of treated rabbits. Conjunctival and corneal damage persisted until the final observation 14 days after treatment.

There are sufficient data showing that the 4 lb/gal EC formulation is a slight primary skin irritant in Albino rabbits.

There are no data on dermal sensitization for this 4 lb/gal EC formulation.

There are sufficient data to show that the 25% EC is a primary eye irritant. In a study done with rabbits three out of nine animals had corneal opacity and conjunctival irritation that persisted for at least seven days. However, there are no data available to assess the acute oral, acute dermal and acute inhalation toxicity as well as the primary skin irritation and skin sensitization of this formulation.

Wettable Powder/Dust Formulation

See data gaps identified for the wettable powder products.

Granular Formulation

Sufficient data are available to show that the acute oral LD_{50} for Terrazole 5% G is greater than 15,380 mg/kg. Signs of toxicity in animals receiving the higher doses included hypoactivity, diarrhea, muscular weakness, nasal discharge, diuresis, emaciation and high stance. Minor pathological changes were observed in the animal that died during the study while the survivors showed no gross pathological alterations.

There are sufficient data to show that the acute dermal LD_{50} for the Terrazole 5% G is greater than 16,000 mg/kg. No mortalities were observed when rabbits were administered this dose on abraded and non-abraded skin. Barely perceptible erythema and slight edema were observed at 24 hours and slight desquamation was reported at 7 and 14 days. Necropsy revealed no gross pathologic alterations.

Sufficient data are available to assess the acute inhalation toxicity of the Terrazole 5% G. In a study testing five male and five female rats exposed for four hours to a dust concentration of 2.33 mg/k of the test material, no deaths were reported.

There are sufficient data to show that the 5% G formulation is not a primary skin irritant. Only minimally irritating erythema was observed when the test material was applied to the abraded and non-abraded skin of rabbits. This irritation cleared by 72 hours.

Sufficient data are also available to show that the 5% G produces mild eye irritation when instilled into the eyes rabbits. In this study, conjunctival irritation was observed in the washed and unwashed eyes of rabbits. This irritation cleared by 48 hours in washed eyes and by 7 days in unwashed eyes.

There are no data on dermal sensitization for this formulation.

TOXICITY HAZARD ASSESSMENT

Manufacturing-Use

The technical material has moderate acute oral toxicity. No effects on reproduction or growth and development have been observed experimentally. No teratogenic effects have been reported, but one of two studies requires validation by the Agency. No mutagenic activity was noted in bacteria exposed to Terrazole, and sufficient data are not available to assess the oncogenic potential of the fungicide.

Emulsifiable Concentrate

These formulations have moderate acute oral and high acute dermal toxicity. The high percentage of petroleum distillates in these formulations makes them irritating to the eyes and skin. If oral ingestion should occur the attending physician should be advised of the petroleum distillate content of these formulations prior to administration of emergency treatment.

Wettable Powder Formulation

These formulations have moderate acute oral toxicity and high acute dermal toxicity. There are no data available on primary eye or skin irritation and skin sensitization for these formulations. However, skin and eye contact should be avoided.

Granular Formulations

The granular formulation has low acute oral toxicity and moderate acute dermal toxicity. Its acute inhalation toxicity is moderate. This formulation is moderately irritating to the eyes and slightly irritating to the skin.

GENERIC DATA GAPS

Manufacturing-Use Terrazole	Guideline Sections
Acute Inhalation Toxicity	163.81-3
Primary Dermal Irritation	163.83-5
Subchronic 21-day Dermal Toxicity	163.82-2
Dermal Sensitization	163.81-6
Oncogenicity Studies (Rats and Mice)	163.83-2
Teratology in Second Species	163.83-3

Mutagenicity Studies (mammalian *in vitro* cytogenetics and heritable translocation or dominant lethal and primary DNA damage assays are needed - the last requirement can be satisfied by sister chromatid exchange or unscheduled DNA synthesis studies	163.84-1

Wettable Powder and Wettable Powder/Dust Formulations

Acute Inhalation Toxicity	163.81-3
Primary Eye Irritation	163.81-4
Primary Dermal Irritation	163.81-5
Dermal Sensitization	163.81-6

Granular Formulation

Dermal Sensitization	168.81-6

Emulsifiable Concentrate Formulations

Terrazole 4 lb/gal

Acute Inhalation Toxicity	163.81-3
Dermal Sensitization	163.81-6

Terrazole 25 EC

Acute Oral Toxicity	163.81-1
Acute Dermal Toxicity	163.81-2
Acute Inhalation Toxicity	163.81-3
Primary Dermal Irritation	163.81-5
Dermal Sensitization	163.81-6

SUGGESTED LABELING

The warning statement on the label for Terrazole 25% Wettable Powder should be rewritten to conform with that on the labels of the other formulation. It should read as follows:

> WARNING--
> KEEP OUT OF REACH OF CHILDREN
>
> Harmful if swallowed. Do not inhale spray mist. Do not get on skin or in eyes. Do not take internally. May cause skin irritation. Wash thoroughly all exposed skin. In case of eye contact flush with plenty of water. Repeated contact may be harmful. Wash thoroughly all contaminated clothing before reuse. Do not store near heat or open flame. Use with adequate ventilation. Keep container closed. Do not contaminate feed or foodstuffs.

Appendix

	Toxicity Categories			
Hazard Indicators	I	II	III	IV
Oral LD_{50}	Up to and including 50 mg/kg	From 50-500 mg/kg	From 500-5000 mg/kg	Greater than 5000/mg/kg
Inhalation LC_{50}	Up to and including 0.2 mg/liter	From 0.2-2 mg/liter	From 2-20 mg/liter	Greater than 20 mg/liter
Dermal LD_{50}	Up to and including 200 mg/kg	From 200-2000 mg/kg	From 2,200-20,000 mg/kg	Greater than 20,000 mg/kg
Eye Effects	Corrosive; corneal opacity not reversible	Corneal opacity reversible within 7 days	No corneal opacity; irritation reversible within 7 days	No irritation
Skin Effects	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours or no effect

BIBLIOGRAPHY

GS009-030--Anon, 1978. Skin sensitization Test with Terrazole Techncal in Guinea Pigs; IBT #8530-10903.

GS009-031--Anon, 1979, Eye Irritation Test in Rabbits. Scientific Associates, Inc.; 6200 S. Lindebergh St, St. Louis, MO 63123.

00001591--Carson, S. 1964. Test for Acute Inhalation Toxicity in Rats. Report (unpublished study received 12/16/64 under 1258-740, prepared by Food and Drug Research Labs, Inc. for Squibb Institute; submitted by Olin Mathieson Chemical Corp., Stamford, Conn.

05004729--Dalvi, R.R. and Howell, C.D. 1977. Toxic Effects of a Fungicide, (Terrazole) on the Hepatic Drug Metabolizing Enzyme System in Mice. Bulletin Environ. Contam. Toxicol. 17-225-232 (MRID 05004729).

0000182--Dreir, H. Horath, L.L., and Lindberg, D.C. 1978. Aerosol Inhalation Study with Terrazole Fungicide 4 lb., Emulsifiable in Albino Rats. IBT #8562-10907. unpublished study received 11/15/78; under 6E1747 prepared by IBT Labs, Inc. submitted by Olin Corp., Stamford, CN.

00001831--Duhamel, C.G. and Poa, H. 1978. Report to Olin Corp. Acute Dermal Toxicity Study with Terrazole Fungicide (4 lb. Emulsifiable) in Albino Rabbits, P.O. # RC-38830. IBT # 8530-10906. (Unpublished study received 11/15/78, under 6E1747, prepared by IBT Labs, Inc.

GS0009-032--Ercegovich, C.D., and K.A. Rashid 1977. The Mutagenic Evaluation of Terrazole for Mutagenic Effects in Bacterial Test Systems. Unpublished data from Pesticide Research Laboratory, PA, State University, University Park, PA. EPA Accession #240890.

GS0009-033--Knickerbocker, M. and Re, T.A. 1979. Teratologic Evaluation of Terrazole Tech. in Dutch-belted Rabbits (Unpublished). No F/MID#. Lab #5845 received 7/6/78.

00001597----Kuchar, E.J. 1970a. Determination of Terrazole Residues in Beagle Dog Tissues, CASR-2-70. Includes method date 2/13/70. (Unpublished study received 3/28/70)

00001601----Kuchar, E.J. 1970b. Analytical Studies--Terrazole ( ) in Simulated Gastric Juice CASR-2-70. (Unpublished study received 5/28/70 under OF0997, submitted by Olin Corp., Stamford, Conn.

00001600--Larson, P.S 1963(a) Toxicology Studies on the Effect of Adding OM-2424 to the Diet of Albino Rats. (Unpublished study including letter dated 9/3/63 from P.S. Larson to Sylvan I. Cohen, received 12/16/64 under 1258-740, prepared by Medical College of Va., Dept of Pharmacology, submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001605--Larson, P.S. 1963(b) Toxicological Studies on the Effect of Adding OM-2424 to the Diet of Beagle Dogs: Three Month Study. (Unpublished study received Dec. 16, 1964, under 1258-741); prepared by Medical College of VA.; Dept. of Pharm, Olin Mathieson Chem. Corp. Stamford, CN.; CDL: 050922.

00001588--Larson, P.S. 1963(c) Toxicologic Studies on the Effect of Adding Olin 2424 to the Diet of Mongrel Dogs: Range Finding Studies (4 weeks). (Unpublished study including addendum and letter dated June 17, 1963, from 1258-740; prepared by Medical College of VA.; Dept. of Pharm., submitted by Olin Mathieson Chem. Corp. Stamford, CN.

00002227--Larson, P.S. and Borzelleca, J.F. 1964(a) Acute Percutaneous Toxicity of Olin 2424 in Albino Rabbits (Olin 2424-9-0, Technical). (Unpublished study including letter to Sylvan I. Cohen, received Dec. 16, 1964, under 1258-740; prepared by Medical College of VA, Dept. of Pharm., submitted by Olin Mathieson Chemical Co., Stamford, CN.

00001590--Larson, P.S. and Borzelleca, J.F. 1964(b) Eye Irritation Properties of Olin 2424 in Rabbits (Olin 2424-9-0, Technical). (Unpublished study including letter dated Nov. 17, 1964, under 1258-740; prepared by Medical College of VA, Dept. of Pharm, submitted by Olin Mathieson Chem. Corp., Stamford, CN.

00001571--Larson, P.S. and Borzelleca, J.F. 1965 The Percutaneous Toxicity to Rabbits (Abraded skin) of Olin Compound 2424 (Olin 2424-9-0, Technical). (Unpublished study including letter dated Jan. 11, 1961, under 1258-Q; Prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001555--Larson, P.S. and Borzelleca, J.F. 1967. Acute Oral Toxicities and Potentiation Studies of Terrachlor and Terrazole in Male Albino Rats. (Unpublished study prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001697--Larson, P.S. and Borzelleca, J.F. 1968(a) Toxicological Study on the Effect of Adding Terrazole to the Diet of Beagle Dogs for a Period of Two Years. (Unpublished study received Nov. 18, 1968, under 0F0997;prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001698--Larson, P.S. and Borzelleca, J.F. 1968(b). Three Generation Reproduction Study on Rats Receiving Terrazole in Their Diet. (Unpublished study received June 9, 1970, under 0F0997; prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001792--Larson, P.S. and Borzelleca, J.F. 1970. Acute Oral Toxicity of Terrazole in Male Albino Rabbits. (Unpublished study received June 9, 1970, under 0F0907; prepared by Medical College of Virginia, Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001599--McKennis, H., Jr., Bowman, E.R. and Dar, M.S. 1970. Studies on the Physiological Disposition of Terrazole-^{14}C. (Unpublished study received May 28, 1970, under 0F0997; prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Corp., Stamford, CN.

00001589--Medical College of Virginia, Department of Pharmacology. 1963. Toxicologic Studies on the Effect of Adding Olin-2424 to the Diet of Albino Rats: Range-Finding Studies (3 weeks). from P.S. Larson to Sylvan I. Cohen, received Dec. 16, 1964, under 1258-740; submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001586--Miller, M. 1961. Acute Oral Toxicity in Mice: Ph. 425/B. (Unpublished study received Dec. 16, 1964, under 1258-740; submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001593--Millstein, L. 1961 Experimental Pesticides 1306 and 2424 (SQ542424): Acute Dermal Toxicity in Rabbits: TH. 08/B. (Unpublished study including letter dated Oct. 26, 1961, from L. Millstein to J.W. Poutsiaka, received Dec. 16, 1964, under 1248-70, submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001592--Moulton, R.H. 1970(a) Acute Oral Toxicity (LD_{50}) Study in Rats. Truban 30% W.P.: S.A. No. R-5719a. (Unpublished study received Oct. , 1970 under 372-43; prepared by Scientific Associates, Inc. Submitted by Mallinckrodt Chemical Works, St. Louis, MO.

00001593--Moulton, R.H. 1970(b). Acute Dermal Toxicity (MLD) in Rabbits; Truban 30% W.P.: S.A. No. R-5719b. (Unpublished study received Oct. 1970 under 372-43; prepared by Scientific Associates, Inc., submitted by Mallinckrodt Chemical Works, St. Louis, MO.

GS0009-034--Nham, Dan, et al. 10/27/77. Acute Oral Toxicity of 5G in Rats. Acute Dermal, Eye Irritation and Primary Skin Irritation Tests of Terrazole 5G in Rabbits.

00001557--Olin Corporation. 1965. Metabolism of Olin 2424 in Mongrel Dogs: CASR-10-65. Includes method dated Nov. 17, 1965. (Unpublished study received Nov. 17, 1965 (?), under 1258-Q.

00001828--Palanker, A.L., and Goldhamer, R.E. 1973. Acute Oral LD_{50} in Rats Primary Dermal Irritation in Rabbits: Terrazole: A-851. (Unpublished study received Nov. 15, 1978, under 6E1747; prepared by Biometric Testing, Inc., submitted by Olin Corp., Stamford, CN.

00001830--Scibor, G. 1978. Report to Olin Corporation: Eye Irritation Studies Irritation Studies with Terrazole Fungicide in Albino Rabbits: P.O. No. 388300: IBT No. 8530-10906. (Unpublished study received Nov. 15, 1978, under 6E1747; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Olin Corp., Stamford, CN.

GS0009-035--Weaver, J. and John W. Grade and D.J. Sullivan 11/2/77. Acute Dust Inhalation Toxicity Study of Terrazole 5G in Rats.

GS0009-036--Webig, J.H., Kennedy, G.L., Jr., Knickerbocker, M., and Smith, S. 1980 Teratologic Evaluation of Etridiazol in Rats and Rabbits. (Unpublished)

Chapter 6

RESIDUE CHEMISTRY

The Proposed Guidelines for Residue Chemistry have not been finalized thus there are no citations for the types of data normally required to assess the Residue Chemistry for Terrazole. However, the Agency must have enough data for each product to assure that the residues of the technical formulation and its metabolites have been adequately identified.

Topical Discussions

Metabolism in Plants
Metabolism in Animals
Analytical Methods
Residue Data
Present Tolerances
Regulatory Incidents

The only formulations used on food crops are Terrazole 5% G and Terrazole 4 lb/gal Emulsifiable.

Metabolism in Plants

The absorption, distribution and metabolic fate of Terrazole was investigated thoroughly. In a study by Dr. McKennis, Jr., (1974, 00001689) cotton plants were grown for periods up to 44 days in soil treated with Terrazole-3-^{14}C at levels up to 260 ppm. (This latter level is more than 100 times the level expected in actual agricultural practice). This study also included laboratory investigations on homogenates of fresh, young cotton plants grown in untreated soil and incubated with Terrazole-3-^{14}C.

Isotopic dilution studies were conducted on cotton plant extracts. Radioactivity determinations were made by scintillation counting and residues were identified by paper chromatography and/or thin layer chromatography (TLC). Residues of Terrazole per se, were further determined by gas liquid chromatography. Distribution of radioactivity in samples taken at 26 and 44 days indicates the presence of Terrazole, trichloroacetic acid, and trace amounts of oxalic acid as metabolites in the plant. Radioactive CO_2 was also detected thus indicating cleavage of the thiadiazole ring. No other metabolites contained the thiadiazole ring.

Another metabolism study by Dr. McKennis (1970, 00001599) with lettuce and potato plants was made using radioactive Terrazole-^{14}C labeled either in the 3-position in the thiadiazole ring or in the 1 position of the ethoxy group.

In both studies, the aqueous plant homogenate was incubated for 24 hours with the labeled compound. Extracts were treated with propanol, filtered, and the reaction product identified by T.L.C. Terrazole per se and the mono-acid were found; the presence of the di-acid as a minor metabolite was also indicated.

In other studies (Kuchar, 1971, 00002255), technical Terrazole was added to the soil, mixed well and allowed to remain at room temperature for three weeks. The soil was then extracted with acidified water, the residue partitioned into chloroform, the chloroform extract evaporated to dryness and the residue examined by mass and/or infrared spectroscopy. Again, the predominant metabolite found was the mono-acid and a small amount of the di-acid (i.e., 3-carboxy-5-hydroxy-1,2,4-thiadiazole) was found. Another compound present at a low levels was 3-carbethoxy-5-ethoxy-1,2,3-thiadiazole. The researchers believed, however, that the latter compound could have been formed either during the extraction process or by rearrangement during mass spectroscopy and may not have been a true metabolite.

In addition, the hydrolytic stability of the mono- and di-acid metabolites was studied (Kuchar, 1970, GS0009-003). Both compounds decomposed completely in one hour in either dilute acid or base at 100°C. The odor of H_2S, indicative of cleavage of the thiadiazole ring, was noted. No identification of the decomposition products was made.

Soil treated at the time of planting of cotton produced no detectable residues of Terrazole per se in the various portions (except leaves) of the mature plant. No detectable residues were found in roots, stems, or bolls at 86 and 158 days after treatment. Residues of 0.1 ppm or less were found in the leaves. No analysis of the metabolites was made in these studies.

The mono-acid is found to be the primary metabolite formed during the degradation of Terrazole in cotton, with the possible formation of the di-acid. Trichloroacetic acid, oxalic acid and carbon dioxide are final degradation products. The metabolism and pathways of degradation for Terrazole in the cotton plant and/or similar agricultural crops are considered adequately defined. The predominant residues in cotton plants which are open to toxicological consideration are Terrazole per se and its mono-acid.

With regard to the residues of Terrazole and its mono-acid metabolite, there are no data available on the fate of Terrazole in avocados or avocado trees. The Agency does have data on the fate of Terrazole in cotton plants and since the Agency does not usually require residue studies on such minor crops as avocados, it is concluded that Terrazole per se and its mono-acid metabolite and also residues in avocados.

Metabolism in Animals

No ^{14}C-radiotracer study involving the ingestion of Terrazole by large ruminants (cows, goats) was submitted. From various feeding studies with rats, rabbits and dogs using radio-labeled material, it was indicated that the metabolism of Terrazole in animals apparently proceeds in a manner similar to that in plants, with conversion to the mono-acid metabolite.

There is also evidence of a minor de-ethylation reaction which leads to the elimination of respiratory radioactive CO_2. The cleavage and fragmentation of the thiadiazole ring to one carbon components appears to occur as a minor metabolic route. Since the registered avocado use has no animal feeding implications (i.e., no likelihood of residues in meat, milk, poultry and eggs), feeding studies are presently not required.

Analytical Methods

The residue data submitted for avocados were obtained by the use of methods CAM-23-73. (Griffith, 1976, 00001645; 1973, 00001570), Olin method CAM-23-75, "Determination of Terrazole by blending with hexane." After filtering, the extract is cleaned up on a Florisil column and a determination of the compound is made by electron capture gas chromatography. The sensitivity is claimed to be 0.005 ppm, however, only two recovery values of 74 percent and 104 percent at fortification levels of 0.06 ppm and 0.3 ppm Terrazole are reported. This method was validated in EPA laboratories for Terrazole on cottonseed at 0.1 ppm and 0.2 ppm. Recoveries ranged from 76 percent to 88 percent. The sensitivity of the method is 0.02 ppm.

Residues of the mono-acid were determined by a liquid chromatographic method (CAM-37-75) (Thomas, 1975, GS-0009-005; Kuchar, 1976, GS-0009-006). This method, however, is intended for the analysis of mono-acid residues in soils and involves extraction of the residue with methanolic ammonium hydroxide. Terrazole is extracted from this solution with hexane. Chloroform is used to extract the mono-acid. After the chloroform is evaporated, the residue is taken up in water and determined by liquid chromatography with a ultra violet detector. Only one recovery value is reported for the mono-acid added to avocados. This value is 80 percent at a fortification level of 0.2 ppm. The sensitivity of the method is regarded as 0.05 ppm.

A polorgraphic method is available that determines residues of the mono-acid (CAM-10-70). This method was subjected to a method trial in EPA laboratories on cottonseed. Levels of fortification were 0.20 ppm and 0.40 ppm of mono-acid with recoveries reportedly ranging from 66 percent to 83 percent. The sensitivity of the method involves extraction of the residue from the crop with acetone by blending. After filtering of the extract, 5% HCl is added to the acetone filtrate and it is shaken in a separatory funnel. The HCl extract is collected and extracted twice with chloroform which is then discarded. Sodium sulfate is added to the HCl extract and it is extracted five times with chloroform. Chloroform portions are combined and evaporated to dryness. The residue is transferred with chloroform to a Florisil column for final clean-up. The column is eluted with methanol and evaporated to dryness. The final residue is taken up in 3N HCl and the concentration of mono-acid determined by polarography.

In conclusion, the above available methods have adequate specificity and are judged satisfactory for enforcement purposes and for data gathering.

Residue Data

Field residue data for avocados should reflect the proposed use with respect to dosage rate, mode of application, number and timing of treatments, formulations used and geographic areas represented.

For the control of avocado root rot Terrazole is to be applied evenly to the soil surface surrounding the trees, in a circular area extending out to the drip line. The amount of material applied to each tree will be governed by the area covered. The application rate for the E.C. formulation is 0.25 oz. for a 5' diameter, 1 oz. for 10', 25 ozs. for 15' and 4.3 oz. for 20' diameter dripline. The granular formulation is applied at essentially the same rates for the various tree sizes.

Following application of either EC or the granular formulation, water is applied to the treated area at the rate of one gallon/square foot. Applications are made once a month for 9-10 months during the growing season.

The label also indicates that the use of Terrazole is intended for distribution and use in California only. No treatments are to be made within 30 days of harvest; and, during application, care should be exercised so that the pesticide does not come in contact with the fruit.

Residue data have been submitted for California grown avocados for the 1974 and 1975 crop years. These data reflect multiple treatments over a 2-4 year period. For the 5% granular formulation, 49 ozs. covering 176 square feet within a 15 foot diameter drip line were applied once each month for 9-10 months during the growing season. Following each application, one gallon of water per square foot of area was applied. For the Terrazole 4 E.C. formulation, 5.0 ozs. covering 176 square feet for a 15 foot diameter drip line were applied once each month for 9-10 months. Following each application, one gallon of water per square foot of area treated was applied. The size of the trees treated ranged from 66-77 cm in diameter of trunk at the base and 18-20 feet in height. The trees were fully mature and fully branched.

The residue studies (Kuchar, 1975, GS0009-007) show no detectable residues in the avocados. These studies also show that there is build-up of residues in avocado trees over the 2-3 year treatment period. It is indicated that if (1) Terrazole is applied to the soil according to label recommendations and does not come in contact with the fruit or foliage of the trees, (2) the skirt of limbs is 3-5 feet above the ground, (3) ripe avocados are harvested by hand or by using a hand pruning-type harvester and (4) the normal time period between the last application and harvest is about 30 days, then the resulting combined residues of Terrazole and its mono-acid metabolite will not exceed the 0.15 ppm established tolerance. (The tolerance is based on method sensitivity which is 0.15 ppm).

Residues in Meat, Milk, Poultry and Eggs

The registered use of Terrazole on avocados does not result in residues of Terrazole or its mono-acid metabolite in meat, milk, poultry or eggs.

Present Tolerances

According to 40 CFR 180.370, a tolerance has been established for combined residues of the fungicide 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole and its mono-acid metabolite, 3-carboxy-5-ethoxy-1,2,4-thiadiazole in or on avocados at 0.15 ppm.

There is an interim tolerance (40 CFR 180.319) of 0.3 ppm in or on cottonseed for residues resulting from the use of formulations with multiple active ingredients, one being Terrazole. This Registration Standard only includes formulations with Terrazole as a single active ingredient, consequently the interim tolerance on cottonseed is excluded from this Standard.

Regulatory Incidents

No report was made on any regulatory action taken by FDA with regard to the registered use of Terrazole.

DISCIPLINARY REVIEW:

Residue Chemistry Profile
Reassessment of Established Tolerances
Generic Data Gaps

RESIDUE CHEMISTRY PROFILE

Terrazole is marketed in the US as a soil-fungicide primarily for prevention from root rot. The metabolic fate of Terrazole in plants through absorption, distribution and degradation was investigated thoroughly in the cotton plant. Studies with ^{14}C radioactive ring labeled material indicate Terrazole (5-ethoxy-3-[trichloromethyl]-1,2,4-thiadiazole) evolves through dechlorination into a mono-acid metabolite 3-carboxy-5-ethoxy-1,2,4-thiadiazole which in turn, through de-ethoxylation, evolves into a di-acid metabolite (3-carboxy-5-hydroxy-1,2,4-thiadiazole. It is concluded that some uptake of Terrazole into the plant exists and that Terrazole *per se* and the mono-acid metabolite are the predominant residues in cottonseed. The hydrolytic stability of the mono-acid and di-acid metabolites was studied. Both compounds decomposed completely in one hour in either dilute acid or base at 100^{o}C. The odor of H_2S present was indicative of cleavage of the thiadiazole ring. Other products of degradation found and identified in the ^{14}C radioactive ring labeled Terrazole studies with cotton plants were trichloroacetic acid, oxalic acid and CO_2.

No ^{14}C-radiotracer study involving the ingestion of Terrazole by large ruminants (cows, goats) was reported. From various feeding studies with rats, rabbits and dogs using radiolabeled material, it was indicated that the metabolism in animals apparently proceeds in a similar manner as that in the cotton plant, i.e., conversion to the mono-acid metabolite and further degradation to the di-acid metabolite leading to the elimination of respiratory radioactive CO_2.

Since there are no registered uses which result in feed items containing residues of Terrazole and/or its mono-acid metabolite, ruminant feeding studies are presently not required. There is just one registered use of Terrazole on avocado trees. Two petitions for tolerances for residues resulting from the use of Terrazole on strawberries (PP 8E2083) and on corn and wheat (PP 0F2317 are pending.

Residue studies on avocados indicate no detectable residues for Terrazole and its mono-acid metabolite resulting from the registered use. Adequate methods are available for identification, quantification and regulatory enforcement. The established tolerance of 0.15 ppm is adequate for the combined residues of Terrazole and its mono-acid metabolite in or on avocados which may result from the registered use of Terrazole on avocado trees. There are no records of incidents involving the enforcement of the tolerance.

REASSESSMENT OF ESTABLISHED TOLERANCES

Tolerances have been established for residues of Terrazole on avocados. There are, however, other tolerances which have been approved by the Agency's Toxicology Branch (cottonseed, corn grain and strawberries) but which have not been finalized by the Office of Pesticide Programs because of one or more deficiencies in their respective petitions. It should also be noted that the use on cottonseed involves formulations which include more than one active ingredient. Accordingly, a tolerance reassessment, other than on avocados, would be premature. A complete tolerance reassessment will be performed when a Standard is developed which covers mixtures of Terrazole with other pesticide products.

Based on the established tolerance of 0.15 ppm for combined residues of Terrazole and its mono-acid metabolite in avocados, the theoretical human exposure to residues is calculated to be 0.00007 mg/day. This figure is based on the average adult eating patterns and on the assumption that avocados contain residues which meet the established tolerance level of 0.15 ppm.

The Agency has calculated a Terrazole acceptable daily intake of 2.5×10^{-2} mg/kg/day for avocados. This value is based on a no-observed-effect level (NOEL) of 10 ppm established in a two year dog study (1 ppm = 0.025 mg/kg), and the incorporation of a 100 fold safety factor in translating the data from animal to man.

Based on an acceptable daily intake value of 2.5×10^{-2} mg/kg/day and an average mass of 60 kg for humans, the Agency has calculated a maximum permissable intake of 1.5 mg/day for avocados.

The theoretical maximum residue contribution of Terrazole to the diet is less than the maximum permissable intake (i.e., $7.0 \times 10^{-5} < 1.5 \times 10^{1}$) thus, current tolerance levels appear to be more than adequate.

GENERIC DATA GAPS

None

Bibliography

GS009-003--Kuchar, E.J., 1970 Hydrolytic stability of 3-carboxy-5-ethoxy-1,2,4-thiadiazole and 3-carboxy-5-hydroxy-1,2,4-thiadiazole under alkaline and acid conditions. pg. 0997.

GS009-007--Kuchar, E.J. 1975. Residues of Terrazole and 3-carboxy-5-ethoxy-1,2,4-thiadiazole in avocados, 1974-5 crop. pg. 1747

00001645--Griffith, W.P. 1975. Appendix: Determination of Terrazole^R (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole) in avocado: CASR-19-76. Method CAM-23-75 dated June 12, 1975. (Unpublished study received October 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark.; CDL: 228143-C)

00001570--Griffith, W.P. 1973. Determination of Terrazole^R (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole) and Terrachlor^R (pentachloronitrobenzene) and allied metabolite in plant tissues or harvest samples. Method CAM-24-73 dated July 3, 1975. (Unpublished study received February 4, 1977 under 1258-812; submitted by Olin Corp. Agricultural Div., Little Rock, Ark.; CDL: 95799-M)

00002255--Kuchar, E.J.. 1971. Residues of Terrazole (5-ethoxy-3-trichloromethyl-1,2-4-thiadiazole) and 3-carboxy-5-ethoxy-1,2,4-thiadiazole in immature cotton plants: CASR-2-71. (Unpublished study received July 20, 1971 under OF0997; submitted by Olin Corp., Chemicals Div., New Haven, Conn.; CDL 097540-A)

00001600--Kuchar, E.J. 1970. Analytical studies concerning metabolism of Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole): CASR-5-70. (Unpublished study received May 28, 1970 under OF0997; submitted by Olin Corp., Stamford, Conn.; CDL: 091717-G)

00001689--McKennis, H., Jr. and E. R. Bowman. 1974. Studies on the disposition and metabolism of Terrazole ^{14}C (3-trichloromethyl-5-ethoxy-1,2,4-thiadiazole) in young cotton grown in Terrazole ^{14}C treated soil. (Unpublished study received August 20, 1971 under OF0997; prepared by Medical College of Virginia Dept. of Pharmacology, submitted by Olin Corporation., Stamford, Conn.; CDL: 091717-F)

00002229--Thomas, R.J. 1970. Determination of 3-carboxy-5-ethoxy-1,2,4-thiadiazole in cotton seeds: analytical method. Method CAM-10-70 (Tentative) dated May 21, 1971 form R. F. Philpitt to W. H. Morgan received May 28, 1970 under OF0997: submitted by Olin Corp., Stamford, Conn.; CDL: 091717-AI).

GS0009-005--Thomas, R.J., 1975. The liquid chromatographic determination of 3 carboxy-5-ethoxy-1,2,4-Thiadiazole in avocados.

GS009-006--Thomas, R., 1975. The liquid chromatographic determination of 3-carboxy-5-ethoxy-1,2,4-thiadiazole in soil. pg. 1747.

Chapter 7

ECOLOGICAL EFFECTS

Topical Discussions

The Topical Discussions listed below correspond to the sections in the 'Proposed Guidelines for Registering Pesticides' of July 10, 1978 (Vol. 43, No. 132, 29696). These sections explain the minimum data the Agency requires to assess Terrazole's effect on non-target organisms.

Topical Discussions	Guidelines
Birds	163.71-1, -2
Wild Mammals	163.70-1, -3
Aquatic Invertebrates	163.72-2,
Fish	163.72-1
Ecosystem Effects	163.71-5; 163.72-6

BIRDS

Birds may be exposed to pesticides by feeding directly on the pesticide granules, indirectly feeding on contaminated plants or poisoned invertebrates or animals, or by inhalation when close to sprays and dusts and by dermal contact. Acute oral, dietary and possibly chronic tests on the toxicity of Terrazole to birds are required to support the Registration Standard.

Acute Oral Toxicity

A determination of the single-dose oral LD_{50} is usually required to support the registration of every manufacturing-use product, and of each formulated product intended for outdoor application. This test should be performed for one avian species: a wild waterfowl (preferably the mallard duck, Anas platyrhynchos), or an upland game bird (preferably the bobwhite quail, Colinis virginianus). The species used in this test should be the same as one of the two species used in the avian dietary tests.

Fletcher, (1972, 00003276) studied the effect of Terrazole on bobwhite quail using a 95-97% technical product. The acute oral LD_{50} was 560 mg/kg. This study characterizes Terrazole as slightly toxic to bobwhite quail, and satisfies the Agency requirements for single dose oral toxicity testing for birds.

Another study by Fletcher, 1972 (00002238) with technical Terrazole (95-97 percent) yielded an acute oral LD_{50} of 1640 mg/kg for mallard ducks. Although this study was not considered adequate due to procedural design, the data, as presented, reinforce the above conclusion that Terrazole is slightly toxic to birds.

Subacute Oral Toxicity

A determination of the 8-day subacute dietary LC_{50} (5-day dietary exposure followed by 3-day observation) is required to support registration of all manufacturing-use products and all formulated products intended for outdoor application.

Information regarding the subacute dietary exposure of technical Terrazole to birds is not available.

Chronic Toxicity

Chronic toxicity data (reproductive, and simulated or actual field tests), may be required after information on persistence, degradation rates, and bioaccumulation has been received by the Agency.

WILD MAMMALS

Data on acute toxicity to wild mammals are required to support the registration of a formulated product when (1) the proposed use pattern of the pesticide indicates that wild mammals may be exposed to the pesticide and (2), data in the Toxicology Chapter are not sufficient to assess the potential hazard to wild mammals. The need for mammalian acute toxicity studies has not been demonstrated.

AQUATIC INVERTEBRATES

A determination of the EC_{50} or LC_{50} for aquatic invertebrates is usually required to support the registration of every manufacturing-use product, and for each formulated product intended for outdoor application. This test must be conducted using the technical material. Since no data are provided to satisfy this requirement, a data gap exists.

FISH

A determination of the 96-hour LC_{50} of the technical compound for one cold-water species and one warm-water species is usually required to support the registration of all manufacturing-use products and for each formulated product for outdoor use. A study by Sleight, (1971, 0001703) reported 3.27 ppm as the 96-hour LC_{50} for bluegill, and 1.21 ppm for trout. These data indicate that Terrazole is moderately toxic to both warm and cold water fish. This study fulfills the data requirements for fish toxicity data.

Ecosystem Effects

Full scale field studies are requested only if problems are identified from the first tier tests. As yet, sufficient data are not available to determine the need for these studies. After all the pertinent information has been evaluated, the studies may be necessary.

DISCIPLINARY REVIEW

Ecological Effects Profile
Hazard Assessment
Generic Data Gaps
Suggested Labeling

ECOLOGICAL EFFECTS PROFILE

Manufacturing-Use Terrazole

A few scientifically sound studies are available that identify the toxicity of Terrazole to non-target organisms.

Terrazole at field use doses markedly inhibited nitrification by soil microbes for several weeks. Effects on wastewater treatment microorganisms have not yet been investigated. Acute oral tests on bobwhite quail and mallard ducks indicate that Terrazole is moderately toxic to birds (560 mg/kg and 1640 mg/kg respectively); but, only the study on bobwhite quail satisfies guidelines requirements. Avian dietary studies on Terrazole as a single active ingredient were not available to further investigate the toxicity of Terrazole to birds. A study was not available to characterize technical Terrazole's toxicity to freshwater aquatic invertebrates. A study by Sleight (1971, 00001703) reported a 96 hour LC_{50} for bluegill and trout as 3.27 and 1.21 ppm respectively. These figures indicate a moderate toxicity to fish. Studies on the phytotoxic effects of Terrazole on nontarget terrestrial plants were available from the efficacy tests which examine the effects of the fungicide on protected plants. The studies reviewed did not indicate any phytotoxicity at the levels recommended for use.

Formulated Terrazole

Avian field tests with the formulated products are required when prior studies and a consideration of pertinent data indicate a need for more information. Considering the results of the avian acute oral studies, it is unlikely that a simulated or actual field studies will be necessary.

HAZARD ASSESSMENT

Considering the use pattern, available toxicity data and available fate data, the Agency does not have serious concerns about the safety of non-target organisms. It should be emphasized, however, that all required data are not available and as such, this decision is not final.

GENERIC DATA GAPS

The following are the minimum studies needed to meet data requirements to register Terrazole according to the Proposed Guidelines of July 10, 1978 (43 FR, No. 132, 29696). It must be noted that these Tier I studies are the minimum requirement. Tier II and III studies may be required if an analysis of the Tier I studies indicates problems. These basic studies test the technical material and are used to assess the hazard associated with the use of the formulated products.

For Manufacturing-Use Terrazole:

	Guidelines Section
(1) Subacute dietary LC_{50} (8-day dietary study) on two avian species, an upland game bird (preferably bobwhite quail) and a wild waterfoul (preferably mallard duck).	163.71-1
(2) A EC_{50} or LC_{50} for a fresh-water aquatic invertebrate (preferably Daphnia magna)	163.72-2

For formulated products: None at this time.

The need for chronic avian or aquatic testing can only be assessed after all preliminary toxicity studies and environmental fate exposure data have been received and reviewed.

Suggested Labeling

For all outdoor uses other than aquatic applications, the minimum labeling requirement is "Do not apply directly to lakes, ponds or streams. Do not contaminate water by cleaning of equipment or disposal of wastes."

BIBLIOGRAPHY

05001204--Davis, R.G., and Pinckard, J.A. 1971. Comparative systemic fungicidal activity and phytotoxicity of certain seed and soil fungicides potentially useful for control of cotton seedling diseases. Plant Disease Reptr. 55 (12):1111-1115

00001800--DeNeve, R.T. 1973. Soil Drench Phytotoxicity Test (73-1) of Banrot and Truban 25% E.C. on Selected South Florida Nursery Plants. (Unpublished study including letter dated June 13, 1973 from R.T. DeNeve to Bill W.A. Small, received June 19, 1973 under 372-46; prepared by La Casa Verde, Inc., submitted by Mallinckrodt Chemical Works, St. Louis, MO. CDL:0032-AA)

05006029--Desai, B.G.; Doriswamy, S.; Geypens, M.; Van Assche, C. 1972. Performance of Aatera. (35%-ethoxy-3-trichloromethyl-1,2,4-thiadiazole) in controlling Phythium damping off of tomato, pea and cauliflower. Mededelingen van de Faculteit Landhouwwetenschappen Rijksuniversiteit Gent./Communications of the Faculty of Agricultural Sciences, State University of Ghent. 1 37(2):516-523

00001664--Erecegovich, C.D. 1976. Effects of 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole (Terrazole) on microorganisms and biochemical processes in soil: Report No. E-1/1-76(0). (Unpublished study received October 20, 1976, under 1258-812; prepared by Pennsylvania State University, University Park, Pesticide Research Laboratory; submitted by Olin Corp., Agricultural Div., Little Rock, AR. CDL:228143-AD.)

00002238--Fletcher, D. 1972. Report to Olin Corporation: Acute Oral Toxicity Study with Olin Terrazole, D8364 FCG in Bobwhite Quail: IBT No. J890. (Unpublished study including letter dated January 26, 1972 from J.C. Calandra to John H. Wedig, received March 3, 1972 under 1258-826; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Olin Corporation, Stamford, CT: CDL:005836-B

00001567--Kvien, C. 1975. Nitrification inhibition in soils by Terrazole Master's thesis, Southern Illinois University, Department of Plant and Soil Science. (Unpublished study including report No. 3067, received February 4, 1977, under 1258-812; submitted by Olin Corporation, Agricultural Division, Little Rock, AR CDL-095799-J.)

00002244--Mallinckrodt Chemical Works 1973. Pothos--Root Rot. (Unpublished study received June 12, 1973 under 372-47; CDL:003217-H)

05006097--McCain, A.H.; Byrne, T.G. 1966. Chemical control of Pythium root rot in ornamentals with Dexon and Terrazole. California Agriculture 20(5):14-15

00001633--Miller, H.N. 1970. Soil Mix Phytotoxicity Studies on Foliage Plants (Unpublished study received October 5, 1970 under 372-UG(43); submitted by Mallinckrodt Chemical Works, St. Louis, MO; CDL:003213-Q.

00001627--Miller, H.N. 1970. Soil Mix Phytotoxicity Using M-4 Formulations. (Unpublished study received October 5, 1970 under 372-UG(43); submitted by Mallinckrodt Chemical Works; CDL:003214-K

00001640-- Nichols, L. I. 1970. Phytotoxicity Test of Truban at Herman Lederer Sons, Parkerford, PA. (Unpublished study received October 5, 1970 under 372-UG(43): submitted by Mallinckrodt Chemical Works, St. Louis, MO; CDL:003213-Y

00002231--Raabe, R.D. 1970. African Violet: Toxicity Trial. (Unpublished study received October 5, 1970 under 372-43; Prepared by University of California--Berkeley, submitted by Mallinckrodt, Inc., St. Louis, MO; CDL:003213-S)

00001703--Sleight, B.H., III. 1971. Bioassay Report: Acute Toxicity of Terrazole (D-8364) to Bluegill *(Lepomis machronirus)* and Rainbow Trout *(Salmo gairdneri)*. Unpublished study that includes well water quality analysis p. 13, received November 23, 1971 under 1258-826; prepared by Bionomics, Inc., submitted by Olin Corporation, Stamford, CT; CDL:101583-A)

Chapter 8

REGULATORY RATIONALE

The Agency has determined that the technical and formulated Terrazole^R products covered in this Standard can be registered for sale, distribution and reformulation in the United States. Current registrations will be maintained in effect if registrants fulfill the data gaps, as outlined, in accordance with Agency determined deadlines. New registrations will be granted if applicants agree to submit or cite the data (in compliance with compensation guidelines) listed in Chapter Two of this document. The Agency considers the Terrazole products covered in this Standard registerable because available data do not indicate any unreasonable adverse effects as outlined in 40 CFR 162.11(a).

PRODUCT COMPOSITION STANDARDS

The Agency will consider for registration manufacturing-use and formulated products which contain any percentage of Terrazole as an active ingredient. Manufacturing-use products covered under this Standard may contain at least 95% active ingredient since data submitted are for technical products containing no less than 95% active ingredient. Formulations covered under this Standard may contain the following maximum percentages of Terrazole active ingredient:

Wettable Powders	35%
Emulsifiable Concentrates	25% and 4 lbs./gallon
Wettable Powders/Dust	30%
Granular	5%

The above limits are set according to submitted data on each of the formulations.

ACUTE TOXICITY LIMITS

The Agency will register manufacturing-use grade Terrazole products which have Toxicity Categories I through IV because the use pattern does not indicate possible adverse exposure to the general public and because the pesticide industry can be required by the Occupational Health and Safety Administration to provide safe working conditions.

For formulated products, the Agency will consider any Toxicity Category; however, the available data will limit present registrations to Toxicity Categories no higher than those outlined in Chapter Two. These categories are assigned according to product composition and use patterns. Current use patterns indicate that applicators are at risk from both dermal and inhalation exposure. Appropriate labeling which reflects a formulation's potential harm is developed from Toxicity Categories and provides for proper advisement in the use of Terrazole products. For formulations which are currently lacking toxicity data, the Agency assumes a Category I potential until sufficient data prove otherwise.

USE PATTERNS

Under this Standard, manufacturing-use Terrazole may only be used in the formulation of specific end-use products which contain currently accepted ranges of active ingredient. Formulated products may be used when indicated by product efficacy and in accordance with all label recommendations and restrictions. For food uses, at present Terrazole is only registered for use on avocados and only in California although the Agency has no reason to object to registration in other areas if pest conditions warrant. These formulations are the 5% granular and the 4 lb a.i/gal emulsifiable concentrate.

DATA REQUIREMENTS

All data requirements are specified in Chapter Two of this Standard. The Agency's need for such data is thoroughly discussed in the Proposed Guidelines (43 FR Nos. 132, 163). These Guidelines present both data specifications and a rationale for each data requirement.

REQUIRED LABELING

All required labeling is specified in Chapter Two of this Standard.

Reproduced from best available copy.

Guide to Use of This Bibliography

1. Content of Bibliography. This bibliography contains citations of all the studies reviewed by EPA in arriving at the positions and conclusions stated elsewhere in this standard. The bibliography is divided into 3 sections: (1) citations that contributed information useful to the review of the chemical and considered to be part of the data base supporting registrations under the standard, (2) citations examined and judged to be inappropriate for use in developing the standard, and (3) standard reference material. Primary sources for studies in this bibliography have been the body of data submitted to EPA and its predecessor agencies in support of past regulatory decisions, and the published technical literature.

2. Units of Entry. The unit of entry in this bibliography is called a "study". In the case of published materials, this corresponds closely to an article. In the case of unpublished materials submitted to the agency, the Agency has sought to identify documents at a level parallel to a published article from within the typically larger volumes in which they were submitted. The resulting "studies" generally have a distinct title (or at least a single subject), can stand alone for purposes of review, and can be described with a conventional bibliographic citation. The Agency has attempted also to unite basic documents and commentaries upon them, treating them as a single study.

3. Identification of Entries. The entries in this bibliography are sorted by author, date of document, and title. Each entry bears, to the left of the citation proper, an eight-digit numeric identifier. This number is unique to the citations, and should be called the "Master Record Identifier", or "MRID". It is not related to the six-digit "Accession Number" which has been used to identify volumes of submitted data; see paragraph 4(d)(4) below for a further explanation. In a few cases, entries added to the bibliography late in the review may be preceded by a nine-character temporary identifier. This is also to be used whenever a specific reference is needed.

4. Form of the Entry. In addition to the Master Record Identifier (MRID), each entry consists of a bibliographic citation containing standard elements followed, in the case of materials submitted to EPA, by a description of the earliest known submission. The bibliographic conventions used reflect the standards for the American National Standards Institute (ANSI), expanded to provide for certain special needs. Some explanatory notes of specific elements follow:

   a. Author. Whenever the Agency could confidently identify one, the Agency has chosen to show a personal author. When no individual was identified, the Agency has shown an identificable laboratory or testing facility as author. As a last resort, the Agency has shown the first known submitter as author.

   b. Document Date. When the date appears as four digits with no question marks, the Agency took it directly from the document. When a four-digit date is followed by a question mark, the bibliographer deduced the date from evidence in the document. When the date appears as (19??), the Agency was unable to determine or estimate the date of the document.

c. Title. This is the third element in the citation. In some cases it has been necessary for the Agency bibliographers to create or enhance a document title. Any such editorial insertions are contained between square brackets.

d. Trailing Parenthesis. For studies submitted to us in the past, the trailing parenthesis include (in addition to any self-explanatory text) the following elements describing the earliest known submission.

   (1) Submission Date. Immediately following the word 'received' appears the date of the earliest known submission.

   (2) Administrative Number. The next element, immediately following the word 'under', is the registration number, experimental permit number, petition number, or other administrative number associated with the earliest known submission.

   (3) Submitter. The third element is the submitter, following the phrase 'submitted by'. When authorship is defaulted to the submitter, this element is omitted.

   (4) Volume Identification. The final element in the trailing parenthesis identifies the EPA accession number of the volume in which the original submission ofo the study appears. The six-digit accession number follows the symbol 'CDL', standing for "Company Data Library". This accession number is in turn followed by an alphabetic suffix which shows the relative position of the study within the volume. For example, within accession number 123456, the first study would be 123456-A; the second, 123456-B; the 26th, 123456-Z; and the 27th 123456-AA.

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY

Citations Considered to be Part of the Data Base Supporting Registration Under This Standard

GS0009-037--Martin, H., ad C.R. Worthing, eds. 1977. Pesticide Index: Basic information on the chemicals used as active components of pesticides, 5th ed. British Corp. Protection Council, Worcestershire, England.

GS0009-038-- Pesticide Chemical Use Pattern Profile for Terrazole (0847011). U.S. Environmental Protection Agency, Office of Pesticide Programs, Benefits and Field Studies Division, May 1979.

GS0009-048--Pesticide Process Encyclopedia, 1977, Noyes Data Corp. Park Ridge, New Jersey.

00001553--Olin Corporation. 1977? Terrazole^{R} Technical Grade--Data Sheet (Unpublished study that includes data sheets A. 1-A.2, A.3-A.4, received Feb. 4, 1977 under 1258-812; CDL: 095799-A)

0001556--Olin Corporation. 1966. Technical Data: Terrachlor^{R} Super X: (Terraclor^{R} + Terrazole). (Unpublished study received Jan 1, 1966? under 1258-Q; CDL: 110045-A)

00001760--Olin Mathieson Chemical Corporation. 1964? Chemical and Physical Properties for Terrazole. (Unpublished study received Dec 16, 1964 under 1258-740; CDL: 119218-A)

00002232--Schingh, J.E. 1976. Vapor Pressure Studies of Terrazole^{R} (5-Ethoxy-3-trichloromethyl-1,2,4-thiadiazole): CASR-21-76. (Unpublished study received Oct 10, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark.; CDL: 228143-0)

GS0009-020--Geomet Technologies, Inc., Compilation of Data Related to Exposure to Terrazole, Geomet Technologies, Inc., Rockville, MD, May 14, 1980a.

GS0009-021--Geomet Technologies, Inc., Use Data for Exposure Analysis of Terrazole, Geomet Technologies, Inc., Rockville, MD, July 17, 1980b.

GS0009-070--Sparks, D., Sales Manager, Crop Protection Chemicals, Olin Corp., Little Rock, Ark, personal communication to E.N. Pelletier, BFSD, EPA, Washingto, D.C. March 31, 1980a.

GS0009-071--Sparks, D., Sales Manager, Crop Protection Chemicals, Olin Corp., Little Rock, Ark, personal communication to E.N. Pelletier, BFSD, EPA, Washington, D.C., Aug. 11, 1980b.

00001664--Ercegovich, C.D. 1976. Effects of 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole (Terrazole) on microorganisms and biochemical processes in soil: Report No. E-1/1/76 (O). (Unpublished study received Oct. 20, 1976, under 1258-812; prepared by PA. State Univ., University Park, Pesticide Research Laboratory; sumbitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL: 228143-AD.

05001190--Helling, C.S., D.G. Dennison, and D.D. Kaufman, 1974. Fungicide movement in soil. Phytopath 64(8): 1091-1100.

GS0009-039--Iacoviello, S.A. 1979. Activated sludge test for Terrazole 3-^{14}C (3-trichloromethyl-5-ethoxy-1,2,4-thiadiazole). (Olin Corp. report CASR-14-79, prepared Apr. 12, 1979 by Olin Research Center, Analytical Department, New Haven, CN). (MRID unknown; CDL: 238774)

00001663--Iwan, G.R. 1976. Olin--^{14}C Terrazole channel catfish *(Ictalurus punctatus* Rafinesque), static bioaccumulation study. (Unpublished study received Oct. 20, 1976, under 1258-812; prepared by Union Carbide Corp, Aquatic Environmental Sciences; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL: 228143-AB.)

00001763--Kuchar, E.J. 1972. Residues of Terrachlor, Terrazole and metabolites in soil: CASR-5-72. (Unpublished study including letter dated Oct. 12, 1972, from R.F. Philpitt to P.C. Williams, received Oct. 17, 1972, under 1258-Q; submitted by Olin Corp., New Haven , CN CDL: 120359-A).

00001661--Kuchar, E.J. 1973. Residues of Terrachlor and Terrazole in soil --1972 studies: CASR-19-73. (Unpublished study received Oct. 20, 1976, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark CDL: 228143-X.)

00001659--Kuchar, E.J. 1976. Field soil dissipation studies concerned with Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole: CASR-6-76. (Unpublished study received Oct. 20, 1978, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL: 228142-S.)

00001660--Kuchar, E.J. 1976. Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole) greenhouse studies in soil: CASR-24-76. (Unpublished study received Oct. 20, 1976, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL: 228143-Y).

00001567--Kvien, C. 1975. Nitrification inhibition in soils by Terrazole. Master's thesis, Southern Illinois University, Department of Plant and Soil Science. (Unpublished study including report no. 3067, received Feb. 4, 1977, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL-095799-J.)

00001650--Thomas, R.J. 1975. Analytical investigations concerned with the rate of hydrolysis of Terrazole-C-14: CASR-7-75. (Unpublished study received Oct. 20, 1976, under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL:228143-H.)

00001652--Thomas, R.J. 1975. Analytical investigations concerned with the rate of hydrolysis of Terrazole-C-14: CADR-7-75. Supplement #1. (Unpublished study received Oct. 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL:228143-J.)

00001657--Thomas, R.J. 1976. Laboratory soil metabolism studies concerned with Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole): CASR-7-76. (Unpublished study received Oct. 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL:228143-Q.)

00001655--Thomas, R.J. 1976. Laboratory soil leaching studies concerned with Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole): CASR-4-76. (Unpublished study received Oct. 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark. CDL:228143-M.)

GS009-030--Anon, 1978. Skin sensitization Test with Terrazole Technical in Guinea Pigs; IBT #8530-10903.

GS009-031--Anon, 1979, Eye Irritation Test in Rabbits. Scientific Associates, Inc.; 6200 S. Lindebergh St, St. Louis, MO 63123.

00001591--Carson, S. 1964. Test for Acute Inhalation Toxicity in Rats. Report (unpublished study received 12/16/64 under 1258-740, prepared by Food and Drug Research Labs, Inc. for Squibb Institute; submitted by Olin Mathieson Chemical Corp., Stamford, Conn.

05004729--Dalvi, R.R. and Howell, C.D. 1977. Toxic Effects of a Fungicide, (Terrazole) on the Hepatic Drug Metabolizing Enzyme System in Mice. Bulletin Environ. Contam. Toxicol. 17-225-232 (MRID 05004729).

0000182--Dreir, H. Horath, L.L., and Lindberg, D.C. 1978. Aerosol Inhalation Study with Terrazole Fungicide 4 lb., Emulsifiable in Albino Rats. IBT #8562-10907. Unpublished study received 11/1/78; under 6E1747 prepared by IBT Labs, Inc. submitted by Olin Corp., Stamford, CN.

00001831--Duhamel, C.G. and Poa, H. 1978. Report to Olin Corp. Acute Dermal Toxicity Study with Terrazole Fungicide (4 lb. Emulsifiable) in Albino Rabbits, P.O. # RC-38830. IBT # 8530-10906. (Unpublished study received 11/15/78, under 6E1747, prepared by IBT Labs, Inc.

GS0009-032--Ercegovich, C.D., and K.A. Rashid 1977. The Mutagenic Evaluation of Terrazole for Mutagenic Effects in Bacterial Test Systems. Unpublished data from Pesticide Research Laboratory, PA, State University, University Park, PA. CDL: 240890.

GS0009-033--Knickerbocker, M. and Re, T.A. 1979. Teratologic Evaluation of Terrazole Tech. in Dutch-belted Rabbits (Unpublished). No F/MID#. Lab #5845 received 7/6/78.

00001597----Kuchar, E.J. 1970a. Determination of Terrazole Residues in Beagle Dog Tissues, CASR-2-70. Includes method date 2/13/70. (Unpublished study received 3/28/70)

00001601----Kuchar, E.J. 1970b. Analytical Studies--Terrazole ( ) in Simulated Gastric Juice CASR-2-70. (Unpublished study received 5/28/70 under 0F0997, submitted by Olin Corp., Stamford, Conn.

00001600--Larson, P.S 1963(a) Toxicology Studies on the Effect of Adding OM-2424 to the Diet of Albino Rats. (Unpublished study including letter dated 9/3/63 form P.S. Larson to Sylvan I. Cohen, received 12/16/64 under 1258-740, prepared by Medical College of Va., Dept of Pharmacology, submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001605--Larson, P.S. 1963(b) Toxicological Studies on the Effect of Adding OM-2424 to the Diet of Beagle Dogs: Three Month Study. (Unpublished study received Dec. 16, 1964, under 1258-741); prepared by Medical College of VA.; Dept. of Pharm, Olin Mathieson Chem. Corp. Stamford, CN.; CDL: 050922.

00001588--Larson, P.S. 1963(c) Toxicologic Studies on the Effect of Adding Olin 2424 to the Diet of Mongrel Dogs: Range Finding Studies (4 weeks). (Unpublished study including addendum and letter dated June 17, 1963, from 1258-740; prepared by Medical College of VA.; Dept. of Pharm., submitted by Olin Mathieson Chem. Corp. Stamford, CN.

00002227--Larson, P.S. and Borzelleca, J.F. 1964(a) Acute Percutaneous Toxicity of Olin 2424 in Albino Rabbits (Olin 2424-9-0, Technical). (Unpublished study including letter to Sylvan I. Cohen, received ec. 16, 1964, under 1258-740; prepared by Medical College of VA, Dept. of Pharm., submitted by Olin Mathieson Chemical Co., Stamford, CN.

00001590--Larson, P.S. and Borzelleca, J.F. 1964(b) Eye Irritation Properties of Olin 2424 in Rabbits (Olin 2424-9-0, Technical). (Unpublished study including letter dated Nov. 17, 1964, under 1258-740; prepared by Medical College of VA, Dept. of Pharm, submitted by Olin Mathieson Chem. Corp., Stamford, CN.

00001571--Larson, P.S. and Borzelleca, 1965 The Percutaneous Toxicity to Rabbits (Abraded skin) of Olin Compound 2424 (Olin 2424-9-0, Technical). (Unpublished study including letter dated Jan. 11, 1961, under 1258-Q; Prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001555--Larson, P.S. and Borzelleca, J.F. 1967. Acute Oral Toxicities and Potentiation Studies of Terrachlor and Terrazole in Male Albino Rats. (Unpublished study prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001697--Larson, P.S. and Borzelleca, J.F. 1968(a) Toxicological Study on the Effect of Adding Terrazole to the Diet of Beagle Dogs for a Period of Two Years. (Unpublished study received Nov. 18, 1968, under 0F0997;prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001698--Larson, P.S. and Borzelleca, J.F. 1968(b). Three Generation Reproduction Study on Rats Receiving Terrazole in Their Diet. (Unpublished study received June 9, 1970, under 0F0997; prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001792--Larson, P.S. and Borzelleca, J.F. 1970. Acute Oral Toxicity of Terrazole in Male Albino Rabbits. (Unpublished study received June 9, 1970, under 0F0907; prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001599--McKennis, H., Jr., Bowman, E.R. and Dar, M.S. 1970. Studies on the Physiological Disposition of Terrazole-^{14}C. (Unpublished study received May 28, 1970, under 0F0997; prepared by Medical College of VA., Dept. of Pharm., submitted by Olin Corp., Stamford, CN.

00001589--Medical College of virginia, Department of Pharmacology. 1963. Toxicologic Studies on the Effect of Adding Olin-2424 to the Diet to Albino Rats: Range-Finding Studies (3 weeks). from P.S. Larson to Sylvan I. Cohen, received Dec. 16, 1964, under 1258-740; submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001586--Miller, M. 1961. Acute Oral Toxicity in Mice: Ph. 425/B. (Unpublished study received Dec. 16, 1964, under 1258-740; submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001593--Millstein, L. 1961 Experimental Pesticides 1306 and 2424 (SQ542424): Acute Dermal Toxicity in Rabbits: TH. 08/B. (Unpublished study including letter dated Oct. 26, 1961, from L. Millstein to J.W. Poutsiaka, received Dec. 16, 1964, under 1248-70, submitted by Olin Mathieson Chemical Corp., Stamford, CN.

00001592--Moulton, R.H. 1970(a) Acute Oral Toxicity (LD_{50}) Study in Rats. Truban 30% W.P.: S.A. No. R-5719a. (Unpublished study received Oct. , 1970 under 372-43; prepared by Scientific Associates, Inc. Submitted by Mallinckrodt Chemical Works, St. Louis, MO.

00001593--Moulton, R.H. 1970(b). Acute Dermal Toxicity (MLD) in Rabbits; Truban 30% W.P.: S.A. No. R-5719b. (Unpublished study received Oct. 1970 under 372-43; prepared by Scientific Associates, Inc., submitted by Mallinckrodt Chemical Works, St. Louis, MO.

GS0009-034--Nham, Dan, et al. 10/27/77. Acute Oral Toxicity of 5G in Rats. Acute Dermal, Eye Irritation and Primary Skin Irritation Tests of Terrazole 5G in Rabbits.

00001557--Olin Corporation. 1965. Metabolism of Olin 2424 in Mongrel Dogs: CASR-10-65. Includes method dated Nov. 17, 1965. (Unpublished study received Nov. 17, 1965 (?), under 1258-Q.

00001828--Palanker, A.L., and Goldhamer, R.E. 1973. Acute Oral LD_{50} in Rats Primary Dermal Irritation in Rabbits: Terrazole: A-851. (Unpublished study received Nov. 15, 1978, under 6E1747; prepared by Biometric Testing, Inc., submitted by Olin Corp., Stamford, CN.

00001830--Scibor, G. 1978. Report to Olin Corporation: Eye Irritation Studies Irritation Studies with Terrazole Fungicide in Albino Rabbits: P.O. No. 38830: IBT No. 8530-10906. (Unpublished study received Nov. 15, 1978, under 6E1747; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Olin Corp., Stamford, CN.

GS0009-035--Weaver, J. and John W. Grade and D.J. Sullivan 11/2/77. Acute Dust Inhalation Toxicity Study of Terrazole 5G in Rats.

GS0009-036--Webig, J.H., Kennedy, G.L., Jr., Knickerbocker, M., and Smith, S. 1980 Teratologic Evaluation of Etridiazol in Rats and Rabbits. (Unpublished)

00001645--Griffith, W.P. 1975. Appendix: Determination of Terrazole^R (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole) in avocado: CASR-19-76. Method CAM-23-75 dated June 12, 1975. (Unpublished study received October 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark.; CDL: 228143-C)

00001570--Griffith, W.P. 1973. Determination of Terrazole^R (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole) and Terrachlor^R (pentachloronitrobenzene) and allied metabolite in plant tissues or harvest samples. Method CAM-24-73 dated July 3, 1975. (Unpublished study received February 4, 1977 under 1258-812; submitted by Olin Corp. Agricultural Div., Little Rock, Ark.; CDL: 95799-M)

GS0009-003--Kuchar, E.J., 1970. Hydrolytic stability of 3-carboxy-5-ethoxy-1,2,4-thiadiazole and 3-carboxy-5-hydroxy-1,2,4-thiadiazole under alkaline and acid conditions. pg. 0997.

00001600--Kuchar, E.J. 1970. Analytical studies concerning metabolism of Terrazole (5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole): CASR-5-70. (Unpublished study received May 28, 1970 under OF0997; submitted by Olin Corp., Stamford, Conn.; CDL: 091717-G)

GS009-007--Kuchar, E.J., 1975. Residues of Terrazole and 3-carboxy-5-ethoxy-1,2,4-thiadiazole in avocados, 1974-5 crop. pg. 1747

00002255--Kuchar, E.J.. 1971. Residues of Terrazole (5-ethoxy-3-trichloromethyl-1,2-4-thiadiazole) and 3-carboxy-5-ethoxy-1,2,4-thiadiazole in immature cotton plants: CASR-2-71. (Unpublished study received July 20, 1971 under OF0997; submitted by Olin Corp., Chemicals Div., New Haven, Conn.; CDL 097540-A)

00001689--McKennis, H., Jr. and E.R. Bowman. 1974. Studies on the dispositon and metabolism of Terrazole ^{14}C (3-trichloromethyl-5-ethoxy-1,2,4-thiadiazole) in young cotton grown in Terrazole ^{14}C treated soil. (Unpublished study received August 20, 1971 under OF0997; prepared by Medical College of Virginia Dept. of Pharmacology, submitted by Olin Corporation., Stamford, Conn.; CDL: 091717-F)

00002229--Thomas, R.J. 1970. Determination of 3-carboxy-5-ethoxy-1,2,4-thiadiazole in cotton seeds: analytical method. Method CAM-10-70 (Tentative) dated May 21, 1971 form R. F. Philpitt to W. H. Morgan received May 28, 1970 under OF0997: submitted by Olin Corp., Stamford, Conn.; CDL: 091717-AI).

GS0009-005--Thomas, R.J., 1975. The liquid chromatographic determination of 3-carboxy-5-ethoxy-1,2,4-thiadiazole in avocados.

GS009-006--Thomas, R.J., 1975. The liquid chromatographic determinant of 3-carboxy-5-ethoxy-1,2,4-thiadiazole in soil. pg. 1747.

05001204--Davis, R.G., and Pinckard, J.A. 1971. Comparative systemic fungicidal activity and phytotoxicity of certain seed and soil fungicides potentially useful for control of cotton seedling diseases. Plant Disease Reptr. 55 (12):1111-1115

00001800--DeNeve, R.T. 1973. Soil Drench Phytotoxicity Test (73-1) of Banrot and Truban 25% E.C. on Selected South Florida Nursery Plants. (Unpublished study including letter dated June 13, 1973 from R.T. DeNeve to Bill W.A. Small, received June 19, 1973 under 372-46; prepared by La Casa Verde, Inc., submitted by Mallinckrodt Chemical Works, St. Louis, MO. CDL:0032-AA)

05006029--Desai, B.G.; Doriswamy, S.; Geypens, M.; Van Assche, C. 1972. Performance of Aatera. (35%-ethoxy-3-trichloromethyl-1,2,4-thiadiazole) in controlling Phythium damping off of tomato, pea and cauliflower. Mededelingen van de Faculteit Landhouwwetenschappen Rijksuniversiteit Gent./Communications of the Faculty of Agricultural Sciences, State University of Ghent. 1 37(2):516-523

00001664--Erecegovich, C.D. 1976. Effects of 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole (Terrazole) on microorganisms and biochemical processes in soil: Report No. E-1/1-76(0). (Unpublished study received October 20, 1976, under 1258-812; prepared by Pennsylvania State University, University Park, Pesticide Research Laboratory; submitted by Olin Corp., Agricultural Div., Little Rock, AR. CDL:228143-AD.)

00002238--Fletcher, D. 1972. Report to Olin Corporation: Acute Oral Toxicity Study with Olin Terrazole, D8364 FCG in Bobwhite Quail: IBT No. J890. (Unpublished study including letter dated January 26, 1972 from J.C. Calandra to John H. Wedig, received March 3, 1972 under 1258-826; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Olin Corporation, Stamford, CT: CDL:005836-B

00002246--Mallinckrodt Chemical Works (19??) Pothos--Root Rot. (Unpublished study received June 12, 1973 under 372-47; CDL:003217-H)

05006097--McCain, A.H.; Byrne, T.G. 1966. Chemical control of Pythium root rot in ornamentals with Dexon and Terrazole. California Agriculture 20(5):14-15

00001633--Miller, H.N. 1970. Soil Mix Phytotoxicity Studies on Foliage Plants (Unpublished study received October 5, 1970 under 372-UG(43); submitted by Mallinckrodt Chemical Works, St. Louis, MO; CDL:003213-Q.

00001627--Miller, H.N. 1970? Soil Mix Phytotoxicity Using M-4 Formulations. (Unpublished study received October 5, 1970 under 372-UG(43); submitted by Mallinckrodt Chemical Works; CDL:003214-K

00001640-- Nichols, L. I. 1970. Phytotoxicity Test of Truban at Herman Lederer Sons, Parkerford, PA. (Unpublished study received October 5, 1970 under 372-UG(43): submitted by Mallinckrodt Chemical Works, St. Louis, MO; CDL:003213-Y

00002231--Raabe, R.D. 1970. African Violet: Toxicity Trial. (Unpublished study received October 5, 1970 under 372-43; Prepared by University of California--Berkeley, submitted by Mallinckrodt, Inc., St. Louis, MO; CDL:003213-S)

00001703--Sleight, B.H., III. 1971. Bioassay Report: Acute Toxicity of Terrazole (D-8364) to Bluegill (lepomis machronirus) and Rainbow Trout (Salmo gairdneri). Unpublished study that includes well water quality analysis p. 13, received November 23, 1971 under 1258-826; prepared by Bionomics, Inc., submitted by Olin Corporation, Stamford, CT; CDL:101583-A)

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Judged to be Inappropriate for Use in Developing this Standard

MRID	CITATION
05001692	Attiah, H.H.; Wahba, M.L. (1973) Phosphorus compounds as a cause of an increase in numbers of the flat mite. Pages 193-196, In Proceedings of the 3rd International Congress of Acarology; Aug 31-Sep 6, 1971, Prague.
05001604	Babu, B.H.; Rao, N.V.S. (1968) Search for physiologically active compounds: Part XII. Synthesis and fungistatic activity of 5:6-and 5:8-quinoline quinones. Pages 31-36, In Proceedings-Indian Academy of Science, Section A. Vol. 67. Bangalore, India: Indian Academy of Sciences.
05010147	Bald, J.G.; Paulus, A.O.; Lenz, J.V. (1973) Fungicidal dips for Easter lily bulbs---treatment before shipment. California Agriculture 27(12):8-10.
05001662	Beckman, H.; Garber, D. (1969) Recovery of 65 organophosphorus pesticides from Florisil with a new solvent elution system. Journal of the Association of Official Analytical Chemists 52(2):286-293.
05001663	Benson, W.R. (1969) The chemistry of pesticides. Annals of the New York Academy of Sciences 160(1):7-29.
05002823	Buchenauer, H. (1975) Differences in light stability of some carboxylic acid anilide fungicides in relation to their applicability for seed and foliar treatment. Pesticide Science 6(5):525-535.
05001649	Burchfield, H.P.; Storrs, E.E. (1977) Residue analysis. Pages 463-505, In Antifungal Compounds: Vol. 1. Edited by M.R. Siegel and H.D. Sisler. New York: Marcel Dekker.
05001701	Caswell, R.L. (1969) Report on pesticide formulations. Journal of the Association of Official Analytical Chemists 52(2): 220-221.
05001564	Daines, R.H. (1955) Sweet potato scurf control studies in New Jersey, 1942-1952. Plant Disease Reporter 39(10):739-745.
05001601	Darby, J.F. (1953) Recent developments in the control of the major diseases of unstaked tomatoes grown on the sandy soils of south Florida. Pages 103-107, In Proceedings--Florida State Horticultural Society. (Florida Agricultural Experiment Station Journal series, no. 220)
05003276	Dittmer, D.S., ed. (1959) Handbook of Toxicology. Volume V: Fungicides. Philadelphia, Pa.: W.B. Saunders. (Available from: University Microfilms International, Ann Arbor, MI)
05006656	Dye, G.A. (1975) The application and uses of terrazole soil fungicide. Pages 302-306, In Combined Proceedings of the International Plant Propagators' Society. Vol. 25. Cleveland, Ohio: International Plant Propagators' Society.
05001651	Dye, H.W., inventor; Food Machinery and Chemical Corp., assignee (1956) Composition for controlling growth of fungi comprising dichloronapthaquinone and bentonite sulfur. U.S. patent 2,771,389. Nov 20. 2 p.

05001623	Fitzgerald, G.P. (1957) The control of the growth of algae with CMU. Transactions of the Wisconsin Academy of Sciences, Arts and Letters 46:281-294.
05001650	Fletcher, H.H., inventor; United States Rubber Co., assignee (1947) Manufacture of chlorinated quinones. U.S. patent 2,422,229. Jun 17. 2 p.
05003964	Geypens, M.; Desai, B.G.; Van Assche, C. (1974) Pectolytic and cellulolytic enzymes produced by 3 *Pythium ultimum* isolates in association with 3 fungicides in stem-bases of pea seedlings. Mededelingen van de Faculteit Landbouwwetenschappen, Rijksuniversiteit Gent. [Communications of the Faculty of Agricultural Sciences, State University of Ghent]. 39(2):979-990.
05001658	Guba, E.F. (1954) Control of Fusicoccum peach canker. Pages 69-70, *In* Massachusetts Fruit Growers' Association. Report of the Annual Meeting, No. 60. North Amherst, Mass.: Massachusetts Fruit Growers' Association.
05001628	Hamdi, Y.A.; Moharram, A.A.; Lofti, M. (1974) Effect of certain fungicides on some rhizobia-legume-symbiotic systems. Zentralblatt fuer Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene, Abteilung II 129(3/4):363-368.
05001563	Harris, H.B.; Luttrell, E.S. (1955) Grain sorghum seed treatment tests and diseases in Georgia for 1954. Plant Disease Reporter 39(4):329-331.
05001699	Horn, N.L. (1961) Control of *Botrytis* rot of strawberries. Plant Disease Reporter 45(10):818-822.
05013485	Hopkins, D.L.; Elmstrom, G.W. (1975) Chemical control of fusarium wilt of watermelon. Pages 196-200, *In* Proceedings of the Florida State Horticultural Society. Vol. 88. Lake Alfred, Fla.: Florida State Horticultural Society. (Florida Agricultural Experiment Stations journal series no. 8011)
05009248	Ivy, H.W. (1973) Response of cotton to herbicide and fungicide-insecticide combinations applied at planting. Pages 132-132, *In* Proceedings of the Southern Weed Science Society. Vol. 26. Athens, Ga.: Southern Weed Science Society.
05001643	Jacks, H.; Brook, P.J. (1954) Control of black spot of apples. New Zealand Journal of Science and Technology 36A:78-89.
05001626	Jansen, L.L.; Gentner, W.A.; Hilton, J.L. (1958) A new method for evaluating potential algicides and determination of the algicidal properties of several substituted-urea and *s*-triazine compounds. Weeds 6:390-398.
05001782	Johnson, H.R.; McIntire, M.S. (1975) Pesticide poisoning in children: a review from Children's Memorial Hospital, Omaha, Nebraska from 1960-1973. Part I. Nebraska Medical Journal 60(2):40-43.
05006642	Kappelman, A.J.; Jr.; Buchanan, G.A. (1968) Influence of fungicides, herbicides and combinations on emergence and seedling growth of cotton. Agronomy Journal 60(6):660-662.
05001696	Kinoshita, F.K.; Frawley, J.P.; Keplinger, M.L.; Calandra, J.C. (1976) Relative cholinesterase and aliesterase inhibition in rat and human blood from exposure to an organic phosphate pesticide. Toxicology and Applied Pharmacology 37(1):168.

05011937 Knauss, J.F. (1972) Field evaluation of several soil fungicides for control of *Scindapsus aureus* cutting decay incited by *Pythium splendens*. Plant Disease Reporter 56(12):1074-1077.

05011938 Knauss, J.F. (1977) Soil fungicides for tropical foliage plants—efficacy and other considerations. Pages 340-342, *In* Proceedings of the Florida State Horticultural Society. Vol. 90. Lake Alfred, Fla.; Florida State Horticultural Society. (Florida Agricultural Experiment Stations journal series no. 762)

00002257 Kuchar, E.J. (1971) Residues of 3-Carboxy-5-ethoxy-1,2,4-thiadiazole in Cotton Seed: CASR-3-71. Includes method CAM-11-71 dated Jul 19, 1971. (Unpublished study received Jul 22, 1971 under 0F0997; submitted by Olin Corp., New Haven, Conn.; CDL:097541-A)

05011881 Laski, R.R.; Watts, R.R. (1973) Gas chromatography of organonitrogen pesticides, using a nitrogen-specific detection system. Journal of the Association of Official Analytical Chemists 56(2):328-332.

05001573 Leukel, R.W.; Webster, O.J.; Earhart, R.W. (1956) Seed-treatment tests on sorghum in 1956. Plant Disease Reporter 40(12):1071-1072.

05001558 Leukel, R.W.; Webster, O.J.; Porter, R.H. (1954) Sorghum seed-treatment tests in 1954. Plant Disease Reporter 38(11):769-770.

05001602 Magie, R.O. (1953) Gladiolus corm treatments in the control of fusarium rot. Pages 318-321, *In* Proceedings--Florida State Horticultural Society. Vol. 66. Lake Alfred, Fla.: Florida State Horticulutral Society. (Florida Agricultural Experiment Station Journal series, No. 192)

00001575 Mallinckrodt Chemical Works (1968) Supporting Data: Koban: [Its Use and Efficacy]. (Unpublished study received Mar 31, 1971 under 372-34; CDL:026860-A)

00001765 Mallinckrodt, Incorporated (1970?) Ingredient Statement: [Truban]. (Unpublished study received Oct 5, 1970 under 372-43; CDL:105640-A)

00002243 Mallinckrodt Chemical Works (19??) Composition of Truban. (Unpublished study received Jun 12, 1973 under 372-47; CDL:003217-A)

05001625 Maloney, T.E.; Palmer, C.M. (1956) Toxicity of six chemical compounds to thirty cultures of algae. Water and Sewage Works 103(11):509-513.

05009871 Malzer, G.L.; Randall, G.W. (1976) Nitrification inhibitor (Terrazole) application for corn production at Waseca. Pages 103-104, *In* University of Minnesota Agricultural Extension Service, Soil Series No. 97. Minneapolis, Minn.: University of Minnesota, Agricultural Extension Service.

05010154 Malzer, G.L.; Randall, G.W. (1977) Nitrification inhibitor (Terrazole) application for corn production in southern Minnesota. Pages 108-116, *In* University of Minnesota Agricultural Extension Service, Soil Series No. 99. Minneapolis, Minn.: University of Minnesota, Agricultural Extension Service.

05010153 Malzer, G.L.; Randall, G.W. (1978) Use of Terrazole as a nitrification inhibitor in fall vs. spring nitrogen application programs for corn production in southern Minnesota. Pages 115-118, *In* University of Minnesota Agricultural Extension Service, Soil Series No. 103. Minneapolis, Minn.: University of Minnesota, Agricultural Extension Service.

05001593 McIntosh, D.L. (1971) Dilution plates used to evaluate initial and residual toxicity of fungicides in soils to zoospores of *Phytophthora cactorum*, the cause of crown rot of apple trees. Plant Disease Reporter 55(3):213-216.

05012996 Mills, J.T.; Wallace, H.A.H. (1968) Determination of selective action of fungicides on the microflora of barley seed. Canadian Journal of Plant Science 48(6):587-594.

05001572 Miller, P.M.; Stoddard, E.M. (1956) Field control of grey mold of strawberries. Plant Disease Reporter 40(9):788-789.

05002910 Mitchell, L.C. (1963) Sensitivity tests for 22 different chlorinated organic pesticides by paper chromatography. Journal of the Association of Official Agricultural Chemists 46(6):988-992.

05011939 Muller, G.J.; Linn, M.B.; Sinclair., J.B. (1972) Translocation, disease remission and persistence of thiabendazole and 5-ethoxy-3(trichloromethyl)-1,2,4-thiadiazole in tomato seedlings. Plant Disease Reporter 56(12):1054-1057.

05001624 Nebeker, A.V.; Gaufin, A.R. (1964) Bioassays to determine pesticide toxicity to the amphipod crustacean, *Gammarus Lacustris*. Pages 64-67, *In* Utah Academy of Sciences Proceedings. Vol. 41, Part I. Salt Lake City, Utah: Utah Academy of Sciences, Arts and Letters.

05001594 Neely, D. (1971) Depostion and tenacity of foliage protectant fungicides. Plant Disease Reporter 55(10):898-902.

05001654 Neely, W.C.; Smith, R.C.; Cody, R.M.; McDuffie, J.R.; Lansden, J.A.; Ellis, S.P. (1973) Biological and Photobiological Action of Pollutants on Aquatic Microorganisms. Auburn, Ala.: Water Resources Research Institute, Auburn University. (WRRI Bulletin 9; also available from: NTIS, Springfield, VA; PB-220 167).

05009250 Nelson, D.W.; Sommers, L.E.; Huber, D.M.; Warren, H.L. (1977) Conserving Energy with Nitrification Inhibitors (Energy in Agriculture). Washington, D.C.: National Science Foundation. (National Science Foundation report no. NSF/RA-770243; Purdue University Agricultural Experiment Station journal paper no. 6289; available from: NTIS, Springfield, VA; PB 277 199).

05001639 Newhook, F.. Davison, R.M. (1956) Incorporation of fungicides in fruit-setting sprays for control of *Botrytis* fruit rot in glasshouse tomatoes. I. Introduction and screening trials. New Zealand Journal of Science and Technology 38A:166-176.

05006545 Narayanan, V.L.; Bernstein, J.; Williams, J. (1966) Antifungal-Substituted-3-(trichloromethyl)-1,2,4-thiadiazoles. Journal of Pharmaceutical Sciences 55(2):217-218.

00001688 Olin Chemicals (1971?) Cotton Seed--Residues of 3-Carboxy-5-Ethoxy-1,2,4-Thiadiazole. (Unpublished study received Aug 20, 1971 under OF0997; CDL:091720-A)

05001702 Osweiler, G.D. (1969) Incidence and diagnostic considerations of major small animal toxicoses. Journal of the American Veterinary Medical Association 155(12):2011-2015.

05001575 Palm, E.T.; Young, R.A. (1957) The compatibility of certain organic fungicides and antibiotics in treatment mixtures as indicated by stability and phytotoxicity. Plant Disease Reporter 41(3):151-155.

05001795 Patten, B.M. (1969) Neuropathy induced by hemorrhage. Archives of Neurology 21(4):381-386.

05001711 Pedersen, P.V.; Crooks, M.J.; Brown, K.F. (1977) Method of obtaining drug-macromolecule binding parameters directly from dynamic dialysis data. Journal of Pharmaceutical Sciences 66(10):1458-1461.

05001797 Pond, S.M.; Graham, G.G.; Birkett, D.J.; Wade, D.N. (1975) Effect of tricyclic antidepressants on drug metabolism. Clinical Pharmacology and Therapeutics 18(2):191-199.

05004243 Powell, D. (1957) An evaluation of some of the common fungicides for control of apple scab. Transactions of the Illinois State Horticultural Society and the Illinois Fruit Council 91:28-29.

05001585 Powell, D. (1960) The inhibitory effects of certain fungicide formulations to apple scab conidia. Plant Disease Reporter 44(3):176-178.

05005882 Reilly, J.J.; Klarman, W.L. (1971) Induction of the soybean phytoalexin hydroxyphaseollin wiith fungicides [abstract]. Phytopathology 61(8):907.

05012577 Rowe, R.C.; Beute, M.K.; Wells, J.C.; Wynne, J.C. (1974) Incidence and control of *Cylindrocladium* black rot of peanuts in North Carolina during 1973. Plant Disease Reporter 58(4):348-352.

05001559 Schenider, I.R.; Campana, R.J. (1955) Fungicide tests in 1954 for the control of sycamore anthracnose. Plant Disease Reporter 39(1):64-65.

05006543 Sen, A.B.; Gupta, S.K. (1962) Possible antiamoebic agents. Part XIX. Synthesis of 1,3,4-thiadiazolines and di-1,3,4-thiadiazolines. Journal of the Indian Chemical Society 39(9):628-634.

05001606 Shakra, S.A.; Porter, R.H. (1960) Control of stinking smut (bunt) of wheat in the Middle East. Pages 1-17, *In* American University of Beirut Faculty of Agricultural Sciences. Publication No. 11. Beirut, Lebanon: American University of Beirut.

05001653 Sjoestrand, B.T.L., inventor; (1960) Manufacture of halogenated organic compounds. U.S. patent 2,955,117. Oct 4. 3 p.

05001718 Smith, S.E.; Rawlins, M.D. (1974) Predication of drug oxidation rates in man: lack of correlation with serum gamma-glutamyl transpeptidase and urinary excretion of D-glucaric acid and 6-beta-hydroxycortisol. European Journal of Clinical Pharmacology 7(1):71-75.

05001603 Stall, R.E. (1964) Fungicidal control of *Botrytis cinerea* Pers. ex Fr. on tomato. Pages 242-244, *In* Proceedings--Florida State Horticultural Society. Vol. 77. Lake Alfred, Fla.: Florida State Horticultural Society. (Florida Agricultural Experiment Station Journal series No. 1986)

00001646 Thomas, R.J. (1976) Chemodynamic Parameter of Terrazole(R) (5-Ethoxy-3-Trichloromethyl-1,2,4-Thiadiazole) Partition Coefficient-n-Octanol vs Water: CASR-18-76. (Unpublished study received Oct 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark.; CDL:228143-D)

00001644 Thomas, R.J. (1976) Chemodynamic Parameter of Terrazole(R) (5-Ethoxy-3-Trichloromethyl-1,2,4-Thiadiazole) Water Solubility: CASR-19-76. (Unpublished study received Oct 20, 1976 under 1258-812; submitted by Olin Corp., Agricultural Div., Little Rock, Ark.; CDL:228143-B)

05001700 Tomizawa, C.; Sato, T.; Yoshii, H. (1960) Uptake of fungicides by fungus spores. Nogyo Gijutsu Kenkyusho Hokoku C. [Bulletin of the National Institute of Agricultural Sciences, Series C.] 12:171-180.

05006544 Tripathy, P.B.; Rout, M.K. (1962) Unsymmetrical cyanines derived from thiazoles and thiadiazoles. Journal of the Indian Chemical Society 39(2):103-108.

05006652 Turner, F.T. (1977) Terrazole as a nitrification inhibitor. International Rice Research Newsletter 2(1):11.

05002824 Ulrich, J.T.; Mathre, D.E. (1972) Mode of action of oxathiin systemic fungicides. V. Effect on electron transport system of *Ustilago maydis* and *Saccharomyces cerevisiae* . Journal of Bacteriology 110(2):628-632.

05001787 Vesell, E.S. (1975) Pharmacogenetic factors as determinants of drug activity. Pages 982-988, *In* Neuropsychopharmacology; Proceedings of the IX Congress of the "Collegium Internationale Neuropsychopharmacologicum"; Jul 7-12, 1974, Paris. Amsterdam, Netherlands: Excerpta Medica. (Excerpta Medica International Congress series no. 359)

05001554 Wallen, V.R. (1953) Treatment of vegetable seed for improved emergence. Plant Disease Reporter 37(12):620-622.

05001566 Wallen, V.R.; Bell, W. (1956) Treatment of vegetable seed for improved emergence--1955. Plant Disease Reporter 40(2):129-132.

05009249 Westerman, R.L.; Tucker, B.B. (1977) An evaluation of the effectiveness of Terrazole as a nitrification inhibitor when urea is applied to grain sorghum. Pages 14-16, *In* Oklahoma Agricultural Experiment Station Research Report No. 758. Stillwater, Okla.: Oklahoma State University, Agricultural Experiment Station.

05012625 Wojtowicz, J.A.; Bhutani, S.K.; inventors; Olin Corp., assignee (1975) Ethanolysis of 3-trichloromethyl-5-chloro-1,2,4-thiadiazole employing aqueous base. U.S. patent 3,890,338. June 17. 5 p. Int. Cl. C 07d 91/60; U.S. Cl. 260/302 D.

05002234 Zimmerman, A. (1974) Phylloquinone Epoxide Reductase: Doctoral Dissertation. St. Louis, Mo.; St. Louis University. (Available from: University Microfilms, Ann Arbor, MI, order no. 75-26,348)

OFFICE PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY

Standard Reference Material

Farm Chemical Handbook. (1979) Meister publishing. Willoughby. Ohio.

The Federal Insecticide, Fungicide, and Rodenticide Act, as amended in 1978, 7th U.S. Code, Chapter 135, 61 Statute 163.78 Statute 190.

Pesticide Process Encyclopedia , 1977, Noyes Data Corp., Park Ridge, New Jersey.

Pesticide Index: Basic information on the chemicals used as active components of pesticides. ; Martin, H., and Worthington, C.R., eds., 1977. 5th ed., British Corp. Protection Council, Worcestershire, England

U.S. Environmental Protection Agency (1978a); Proposed Guidelines for Registering Pesticides in the United States. *Federal Register*, 43 (132) 29696.

U.S. Environmental Protection Agency (1978b); Proposed Guidelines for Registering Pesticides in the United States; Hazard Evaluation: Humans and Domestic Animals. Federal Register, 43 (163) 37336.

U.S. Environmental Protection Agency (1980); Regulations for the Enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act, Title 40, Chapter 1, Part 162.

U.S. Environmental Protection Agency (in press) Proposed Guidelines for Registering Pesticides in the United States. Subparts G (Product Performance) and H (Label Development).

*U S GOVERNMENT PRINTING OFFICE: 1980 341-085/3948